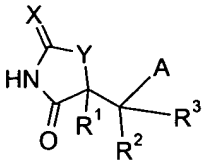
CLAIMS

1. A pharmaceutical composition comprising

insulin and a zinc-binding ligand which reversibly binds to a His^{B10} Zn^{2+} site of an insulin hexamer, wherein the ligand is selected from the group consisting of

benzotriazoles, 3-hydroxy 2-naphthoic acids, salicylic acids, tetrazoles, thiazolidinediones, 5-mercaptotetrazoles, pyrimidinetriones, or 4-cyano-1,2,3-triazoles, or enantiomers, diastereomers, racemic mixtures, tautomers, or salts thereof with a pharmaceutically acceptable acid or base.

2. A pharmaceutical composition according to claim 1 wherein the zinc-binding ligand is



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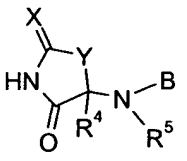

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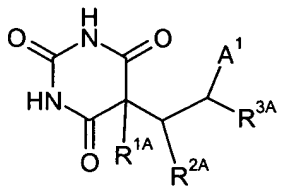


wherein

X is =O, =S or =NH

Y is -S-, -O- or -NH-

R^1, R^{1A} and R^4 are independently selected from hydrogen or C_1-C_6-alkyl,

R^2 and R^{2A} are hydrogen or C_1-C_6-alkyl or aryl, R^1 and R^2 may optionally be combined to form a double bond, R^{1A} and R^{2A} may optionally be combined to form a double bond,

R^3, R^{3A} and R^5 are independently selected from hydrogen, halogen, aryl optionally substituted with one or more substituents independently selected from R^{16}, C_1-C_6-alkyl, or $-C(O)NR^{11}R^{12}$,

A, A^1 and B are independently selected from C_1-C_6-alkyl, aryl, aryl-C_1-C_6-alkyl, $-NR^{11}$-aryl, aryl-C_2-C_6-alkenyl or heteroaryl, wherein the alkyl or alkenyl is optionally substituted with one or more substituents independently selected from R^6 and the aryl or heteroaryl is optionally substituted with up to four substituents R^7, R^8, R^9, and R^{10},

A and R^3 may be connected through one or two valence bonds, B and R^5 may be connected through one or two valence bonds,

R^6 is independently selected from halogen, $-CN$, $-CF_3$, $-OCF_3$, aryl, -COOH and $-NH_2$,

R^7, R^8, R^9 and R^{10} are independently selected from

- hydrogen, halogen, -CN, -CH_2CN, -CHF_2, -CF_3, -OCF_3, -$OCHF_2$, -OCH_2CF_3, -OCF_2CHF_2, -$S(O)_2CF_3$, -$OS(O)_2CF_3$, -SCF_3, -NO_2, -OR^{11}, -$NR^{11}R^{12}$, -SR^{11}, -$NR^{11}S(O)_2R^{12}$, -$S(O)_2NR^{11}R^{12}$, -$S(O)NR^{11}R^{12}$, -$S(O)R^{11}$, -$S(O)_2R^{11}$, -$OS(O)_2$ R^{11}, -$C(O)NR^{11}R^{12}$, -$OC(O)NR^{11}R^{12}$, -$NR^{11}C(O)R^{12}$, -$CH_2C(O)NR^{11}R^{12}$, -OC_1-C_6-alkyl-$C(O)NR^{11}R^{12}$, -CH_2OR^{11}, -$CH_2OC(O)R^{11}$, -$CH_2NR^{11}R^{12}$, -$OC(O)R^{11}$, -OC_1-C_{15}-alkyl-$C(O)OR^{11}$, -OC_1-C_6-alkyl-OR^{11}, -SC_1-C_6-alkyl-$C(O)OR^{11}$, -C_2-C_6-alkenyl-$C(=O)OR^{11}$, -NR^{11}-$C(=O)$-C_1-C_6-alkyl-$C(=O)OR^{11}$, -NR^{11}-$C(=O)$-C_1-C_6-alkenyl-$C(=O)OR^{11}$, -$C(O)OR^{11}$, $C(O)R^{11}$, or –C_2-C_6-alkenyl-$C(=O)R^{11}$, =O, or -C_2-C_6-alkenyl-$C(=O)$-$NR^{11}R^{12}$,

- C_1-C_6-alkyl, C_2-C_6-alkenyl or C_2-C_6-alkynyl, each of which may optionally be substituted with one or more substituents independently selected from R^{13},

- aryl, aryloxy, aryloxycarbonyl, aroyl, arylsulfanyl, aryl-C_1-C_6-alkoxy, aryl-C_1-C_6-alkyl, aryl-C_2-C_6-alkenyl, aroyl-C_2-C_6-alkenyl, aryl-C_2-C_6-alkynyl, heteroaryl, heteroaryl-C_1-C_6-alkyl, heteroaryl-C_2-C_6-alkenyl, heteroaryl-C_2-C_6-alkynyl, or C_3-C_6 cycloalkyl,

of which each cyclic moiety may optionally be substituted with one or more substituents independently selected from R^{14},

R^{11} and R^{12} are independently selected from hydrogen, OH, C_1-C_{20}-alkyl, aryl-C_1-C_6-alkyl or aryl, wherein the alkyl groups may optionally be substituted with one or more substituents independently selected from R^{15}, and the aryl groups may optionally be substituted one or more substituents independently selected from R^{16}; R^{11} and R^{12} when attached to the same nitrogen atom may form a 3 to 8 membered heterocyclic ring with the said nitrogen atom, the heterocyclic ring optionally containing one or two further heteroatoms selected from nitrogen, oxygen and sulphur, and optionally containing one or two double bonds,

R^{13} is independently selected from halogen, -CN, -CF_3, -OCF_3, -OR^{11}, -$C(O)OR^{11}$, -$NR^{11}R^{12}$, and -$C(O)NR^{11}R^{12}$,

R^{14} is independently selected from halogen, -$C(O)OR^{11}$, -$CH_2C(O)OR^{11}$, -CH_2OR^{11}, -CN, -CF_3, -OCF_3, -NO_2, -OR^{11}, -$NR^{11}R^{12}$, -$NR^{11}C(O)R^{11}$, -$S(O)_2R^{11}$, aryl and C_1-C_6-alkyl,

R^{15} is independently selected from halogen, -CN, $-CF_3$, =O, $-OCF_3$, $-OC_1$-C_6-alkyl, $-C(O)OC_1$-C_6-alkyl, -COOH and $-NH_2$,

R^{16} is independently selected from halogen, $-C(O)OC_1$-C_6-alkyl, -COOH, -CN, $-CF_3$, $-OCF_3$, $-NO_2$, -OH, $-OC_1$-C_6-alkyl, $-NH_2$, C(=O) or C_1-C_6-alkyl, or any enantiomer, diastereomer, including a racemic mixture, tautomer as well as a salt thereof with a pharmaceutically acceptable acid or base.

3. A pharmaceutical composition according to claim 2 wherein X is =O or =S.

4. A pharmaceutical composition according to claim 3 wherein X is =O.

5. A pharmaceutical composition according to claim 3 wherein X is =S.

6. A pharmaceutical composition according to claim 2 wherein Y is -O- or -S-.

7. A pharmaceutical composition according to claim 6 wherein Y is -O-.

8. A pharmaceutical composition according to claim 6 wherein Y is -NH-.

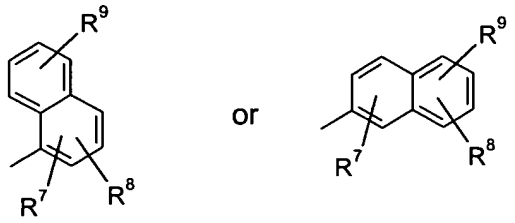
9. A pharmaceutical composition according to claim 6 wherein Y is -S-.

10. A pharmaceutical composition according to claim 2 wherein A is aryl optionally substituted with up to four substituents, R^7, R^8, R^9, and R^{10} which may be the same or different.

11. A pharmaceutical composition according to claim 10 wherein A is selected from ArG1 optionally substituted with up to four substituents, R^7, R^8, R^9, and R^{10} which may be the same or different.

12. A pharmaceutical composition according to claim 11 wherein A is phenyl or naphtyl optionally substituted with up to four substituents, R^7, R^8, R^9, and R^{10} which may be the same or different.

13. A pharmaceutical composition according to claim 12 wherein A is



14. A pharmaceutical composition according to claim 12 wherein A is phenyl.

15. A pharmaceutical composition according to claim 2 wherein A is heteroaryl optionally substituted with up to four substituents, R^7, R^8, R^9, and R^{10} which may be the same or different.

16. A pharmaceutical composition according to claim 15 wherein A is selected from Het1 optionally substituted with up to four substituents, R^7, R^8, R^9, and R^{10} which may be the same or different.

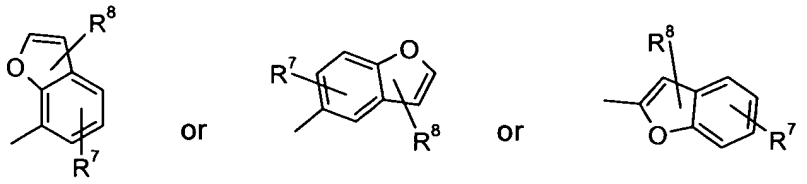
17. A pharmaceutical composition according to claim 16 wherein A is selected from Het2 optionally substituted with up to four substituents, R^7, R^8, R^9, and R^{10} which may be the same or different.

18. A pharmaceutical composition according to claim 17 wherein A is selected from Het3 optionally substituted with up to four substituents, R^7, R^8, R^9, and R^{10} which may be the same or different.

19. A pharmaceutical composition according to claim 18 wherein A is selected from the group consisting of indolyl, benzofuranyl, quinolyl, furyl, thienyl, or pyrrolyl, wherein each heteroaryl may optionally substituted with up to four substituents, R^7, R^8, R^9, and R^{10} which may be the same or different.

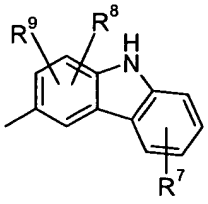
20. A pharmaceutical composition according to claim 18 wherein A is benzofuranyl optionally substituted with up to four substituents R^7, R^8, R^9, and R^{10} which may be the same or different.

21. A pharmaceutical composition according to claim 20 wherein A is



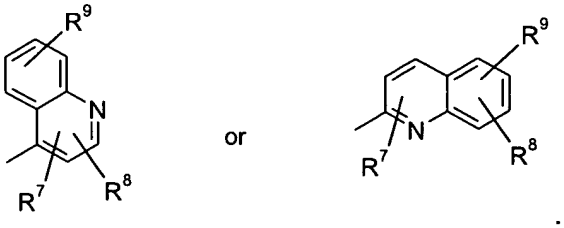
22. A pharmaceutical composition according to claim 18 wherein A is carbazolyl optionally substituted with up to four substituents R^7, R^8, R^9, and R^{10} which may be the same or different.

23. A pharmaceutical composition according to claim 22 wherein A is



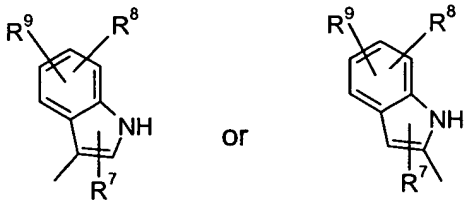
24. A pharmaceutical composition according to claim 18 wherein A is quinolyl optionally substituted with up to four substituents R^7, R^8, R^9, and R^{10} which may be the same or different.

25. A pharmaceutical composition according to claim 24 wherein A is



26. A pharmaceutical composition according to claim 18 wherein A is indolyl optionally substituted with up to four substituents R^7, R^8, R^9, and R^{10} which may be the same or different.

27. A pharmaceutical composition according to claim 26 wherein A is



28. A pharmaceutical composition according to claim 2 wherein R^1 is hydrogen.

29. A pharmaceutical composition according to claim 2 wherein R^2 is hydrogen.

30. A pharmaceutical composition according to claim 2 wherein R^1 and R^2 are combined to form a double bond.

31. A pharmaceutical composition according to claim 2 wherein R^3 is C_1-C_6-alkyl, halogen, or $C(O)NR^{16}R^{17}$.

32. A pharmaceutical composition according to claim 31 wherein R^3 is C_1-C_6-alkyl or $C(O)NR^{16}R^{17}$.

33. A pharmaceutical composition according to claim 32 wherein R^3 is methyl.

34. A pharmaceutical composition according to claim 2 wherein B is phenyl optionally substituted with up to four substituents, R^7, R^8, R^9, and R^{10} which may be the same or different.

35. A pharmaceutical composition according to claim 2 wherein R^4 is hydrogen.

36. A pharmaceutical composition according to claim 2 wherein R^5 is hydrogen.

37. A pharmaceutical composition according to claim 2 wherein R^6 is aryl.

38. A pharmaceutical composition according to claim 37 wherein R^6 is phenyl.

39. A pharmaceutical composition according to claim 2 wherein R^7, R^8, R^9 and R^{10} are independently selected from

- hydrogen, halogen, $-NO_2$, $-OR^{11}$, $-NR^{11}R^{12}$, $-SR^{11}$, $-NR^{11}S(O)_2R^{12}$, $-S(O)_2NR^{11}R^{12}$, $-S(O)NR^{11}R^{12}$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-OS(O)_2\ R^{11}$, $-NR^{11}C(O)R^{12}$, $-CH_2OR^{11}$, $-CH_2OC(O)R^{11}$, $-CH_2NR^{11}R^{12}$, $-OC(O)R^{11}$, $-OC_1$-C_6-alkyl-$C(O)OR^{11}$, $-OC_1$-C_6-alkyl-$C(O)NR^{11}R^{12}$, $-OC_1$-C_6-alkyl-OR^{11}, $-SC_1$-C_6-alkyl-$C(O)OR^{11}$, $-C_2$-C_6-alkenyl-$C(=O)OR^{11}$, $-C(O)OR^{11}$, or $-C_2$-C_6-alkenyl-$C(=O)R^{11}$,

- C_1-C_6-alkyl, C_2-C_6-alkenyl or C_2-C_6-alkynyl, which may each optionally be substituted with one or more substituents independently selected from R^{13}

- aryl, aryloxy, aroyl, arylsulfanyl, aryl-C_1-C_6-alkoxy, aryl-C_1-C_6-alkyl, aryl-C_2-C_6-alkenyl, aroyl-C_2-C_6-alkenyl, aryl-C_2-C_6-alkynyl, heteroaryl, heteroaryl-C_1-C_6-alkyl, wherein each of the cyclic moieties optionally may be substituted with one or more substituents independently selected from R^{14}

40. A pharmaceutical composition according to claim 39 wherein R^7, R^8, R^9 and R^{10} are independently selected from

- hydrogen, halogen, $-NO_2$, $-OR^{11}$, $-NR^{11}R^{12}$, $-SR^{11}$, $-S(O)_2R^{11}$, $-OS(O)_2\ R^{11}$, $-CH_2OC(O)R^{11}$, $-OC(O)R^{11}$, $-OC_1$-C_6-alkyl-$C(O)OR^{11}$, $-OC_1$-C_6-alkyl-OR^{11}, $-SC_1$-C_6-alkyl-$C(O)OR^{11}$, $-C(O)OR^{11}$, or $-C_2$-C_6-alkenyl-$C(=O)R^{11}$,

- C_1-C_6-alkyl or C_1-C_6-alkenyl which may each optionally be substituted with one or more substituents independently selected from R^{13}

- aryl, aryloxy, aroyl, aryl-C_1-C_6-alkoxy, aryl-C_1-C_6-alkyl, heteroaryl,

of which each of the cyclic moieties optionally may be substituted with one or more substituents independently selected from R^{14}

41. A pharmaceutical composition according to claim 40 wherein R^7, R^8, R^9 and R^{10} are independently selected from

- hydrogen, halogen, $-NO_2$, $-OR^{11}$, $-NR^{11}R^{12}$, $-SR^{11}$, $-S(O)_2R^{11}$, $-OS(O)_2\ R^{11}$, $-CH_2OC(O)R^{11}$, $-OC(O)R^{11}$, $-OC_1$-C_6-alkyl-$C(O)OR^{11}$, $-OC_1$-C_6-alkyl-OR^{11}, $-SC_1$-C_6-alkyl-$C(O)OR^{11}$, $-C(O)OR^{11}$, or $-C_2$-C_6-alkenyl-$C(=O)R^{11}$,

- C_1-C_6-alkyl or C_1-C_6- which may each optionally be substituted with one or more substituents independently selected from R^{13}

- aryl, aryloxy, aroyl, aryl-C_1-C_6-alkoxy, aryl-C_1-C_6-alkyl, heteroaryl,

of which each of the cyclic moieties optionally may be substituted with one or more substituents independently selected from R^{14}.

42. A pharmaceutical composition according to claim 41 wherein R^7, R^8, R^9 and R^{10} are independently selected from

- hydrogen, halogen, $-OR^{11}$, $-OC_1$-C_6-alkyl-$C(O)OR^{11}$, or $-C(O)OR^{11}$,

- C_1-C_6-alkyl which may each optionally be substituted with one or more substituents independently selected from R^{13}

- aryl, aryloxy, aryl-C_1-C_6-alkoxy,

of which each of the cyclic moieties optionally may be substituted with one or more substituents independently selected from R^{14}.

43. A pharmaceutical composition according to claim 42 wherein R^7, R^8, R^9 and R^{10} are independently selected from

- hydrogen, halogen, $-OR^{11}$, $-OC_1$-C_6-alkyl-$C(O)OR^{11}$, or $-C(O)OR^{11}$,

- C_1-C_6-alkyl which may each optionally be substituted with one or more substituents independently selected from R^{13}

- ArG1, ArG1oxy, ArG1-C_1-C_6-alkoxy,

of which each of the cyclic moieties optionally may be substituted with one or more substituents independently selected from R^{14}.

44. A pharmaceutical composition according to claim 43 wherein R^7, R^8, R^9 and R^{10} are independently selected from

- hydrogen, halogen, $-OR^{11}$, $-OC_1$-C_6-alkyl-$C(O)OR^{11}$, or $-C(O)OR^{11}$,

- C_1-C_6-alkyl which may optionally be substituted with one or more substituents independently selected from R^{13}

- phenyl, phenyloxy, phenyl-C_1-C_6-alkoxy, wherein each of the cyclic moieties optionally may be substituted with one or more substituents independently selected from R^{14}.

45. A pharmaceutical composition according to claim 2 wherein R^{11} and R^{12} are independently selected from hydrogen, C_1-C_{20}-alkyl, aryl or aryl-C_1-C_6-alkyl, wherein the alkyl groups may optionally be substituted with one or more substituents independently selected from R^{15}, and the aryl groups may optionally be substituted one or more substituents independently selected from R^{16}; R^{11} and R^{12} when attached to the same nitrogen atom may form a 3 to 8 membered heterocyclic ring with the nitrogen atom, the heterocyclic ring optionally containing one or two further heteroatoms selected from nitrogen, oxygen and sulphur, and optionally containing one or two double bonds.

46. A pharmaceutical composition according to claim 45 wherein R^{11} and R^{12} are independently selected from hydrogen, C_1-C_{20}-alkyl, aryl or aryl-C_1-C_6-alkyl, wherein the alkyl groups may optionally be substituted with one or more substituents independently selected from R^{15}, and the aryl groups may optionally be substituted one or more substituents independently selected from R^{16}.

47. A pharmaceutical composition according to claim 46 wherein R^{11} and R^{12} are independently selected from phenyl or phenyl-C_1-C_6-alkyl.

48. A pharmaceutical composition according to claim 46 wherein one or both of R^{11} and R^{12} are methyl.

49. A pharmaceutical composition according to claim 2 wherein R^{13} is independently selected from halogen, CF_3, OR^{11} or $NR^{11}R^{12}$.

50. A pharmaceutical composition according to claim 49 wherein R^{13} is independently selected from halogen or OR^{11}.

51. A pharmaceutical composition according to claim 50 wherein R^{13} is OR^{11}.

52. A pharmaceutical composition according to claim 2 wherein R^{14} is independently selected from halogen, $-C(O)OR^{11}$, -CN, $-CF_3$, $-OR^{11}$, $S(O)_2R^{11}$, and C_1-C_6-alkyl.

53. A pharmaceutical composition according to claim 52 wherein R^{14} is independently selected from halogen, $-C(O)OR^{11}$, or $-OR^{11}$.

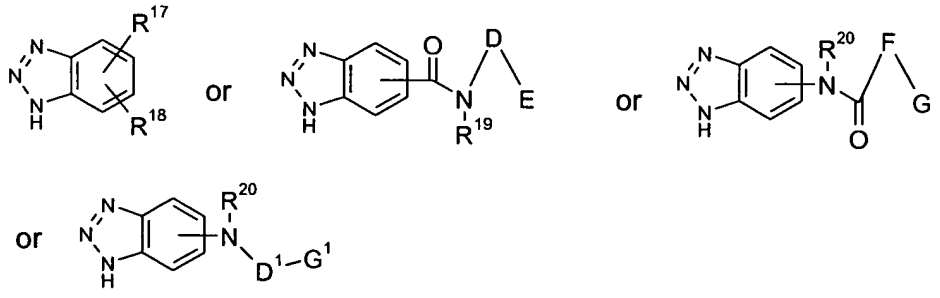
54. A pharmaceutical composition according to claim 2 wherein R^{15} is independently selected from halogen, -CN, $-CF_3$, $-C(O)OC_1$-C_6-alkyl,and –COOH.

55. A pharmaceutical composition according to claim 54 wherein R^{15} is independently selected from halogen or $-C(O)OC_1$-C_6-alkyl.

56. A pharmaceutical composition according to claim 2 wherein R^{16} is independently selected from halogen, $-C(O)OC_1$-C_6-alkyl, -COOH, $-NO_2$, $-OC_1$-C_6-alkyl, $-NH_2$, C(=O) or C_1-C_6-alkyl.

57. A pharmaceutical composition according to claim 56 wherein R^{16} is independently selected from halogen, $-C(O)OC_1$-C_6-alkyl, -COOH, $-NO_2$, or C_1-C_6-alkyl.

58. A pharmaceutical composition according to claim 1 wherein the zinc-binding ligand is



wherein

R^{19} is hydrogen or C_1-C_6-alkyl,

R^{20} is hydrogen or C_1-C_6-alkyl,

D, D^1 and F are a valence bond, C_1-C_6-alkylene or C_1-C_6-alkenylene optionally substituted with one or more substituents independently selected from R^{72},

R^{72} is independently selected from hydroxy, C_1-C_6-alkyl, or aryl,

E is C_1-C_6-alkyl, aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with up to three substituents R^{21}, R^{22} and R^{23},

G and G^1 are C_1-C_6-alkyl, aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with up to three substituents R^{24}, R^{25} and R^{26},

R^{17}, R^{18}, R^{21}, R^{22}, R^{23}, R^{24}, R^{25} and R^{26} are independently selected from

- hydrogen, halogen, -CN, -CH_2CN, -CHF_2, -CF_3, -OCF_3, -$OCHF_2$, -OCH_2CF_3, -OCF_2CHF_2, -$S(O)_2CF_3$, -SCF_3, -NO_2, =O, -OR^{27}, -$NR^{27}R^{28}$, -SR^{27}, -$NR^{27}S(O)_2R^{28}$, -$S(O)_2NR^{27}R^{28}$, -$S(O)NR^{27}R^{28}$, -$S(O)R^{27}$, -$S(O)_2R^{27}$, -$C(O)NR^{27}R^{28}$, -$OC(O)NR^{27}R^{28}$, -$NR^{27}C(O)R^{28}$, -$NR^{27}C(O)OR^{28}$, -$CH_2C(O)NR^{27}R^{28}$, -$OCH_2C(O)NR^{27}R^{28}$, -CH_2OR^{27}, -$CH_2NR^{27}R^{28}$, -$OC(O)R^{27}$, -OC_1-C_6-alkyl-$C(O)OR^{27}$, -SC_1-C_6-alkyl-$C(O)OR^{27}$, –C_2-C_6-alkenyl-$C(=O)OR^{27}$, -NR^{27}-C(=O)-C_1-C_6-alkyl-$C(=O)OR^{27}$, -NR^{27}-C(=O)-C_1-C_6-alkenyl-$C(=O)OR^{27}$, -C(=O)NR^{27}-C_1-C_6-alkyl-$C(=O)OR^{27}$, -C_1-C_6-alkyl-$C(=O)OR^{27}$,or -$C(O)OR^{27}$,
- C_1-C_6-alkyl, C_2-C_6-alkenyl or C_2-C_6-alkynyl,

which may optionally be substituted with one or more substituents independently selected from R^{29},

- aryl, aryloxy, aryloxycarbonyl, aroyl, aryl-C_1-C_6-alkoxy, aryl-C_1-C_6-alkyl, aryl-C_2-C_6-alkenyl, aryl-C_2-C_6-alkynyl, heteroaryl, heteroaryl-C_1-C_6-alkyl, heteroaryl-C_2-C_6-alkenyl or heteroaryl-C_2-C_6-alkynyl,

of which the cyclic moieties optionally may be substituted with one or more substituents selected from R^{30},

R^{27} and R^{28} are independently selected from hydrogen, C_1-C_6-alkyl, aryl-C_1-C_6-alkyl or aryl, or R^{27} and R^{28} when attached to the same nitrogen atom together with the said nitrogen atom may form a 3 to 8 membered heterocyclic ring optionally containing one or two further heteroatoms selected from nitrogen, oxygen and sulphur, and optionally containing one or two double bonds,

R^{29} is independently selected from halogen, -CN, $-CF_3$, $-OCF_3$, $-OR^{27}$, and $-NR^{27}R^{28}$,

R^{30} is independently selected from halogen, $-C(O)OR^{27}$, -CN, $-CF_3$, $-OCF_3$, $-NO_2$, $-OR^{27}$, $-NR^{27}R^{28}$ and C_1-C_6-alkyl, or any enantiomer, diastereomer, including a racemic mixture, tautomer as well as a salt thereof with a pharmaceutically acceptable acid or base.

59. A pharmaceutical composition according to claim 58 wherein D is a valence bond.

60. A pharmaceutical composition according to claim 58 wherein D is C_1-C_6-alkylene optionally substituted with one or more hydroxy, C_1-C_6-alkyl, or aryl.

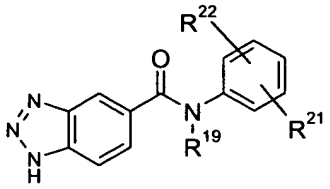
61. A pharmaceutical composition according to claim 58 wherein E is aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with up to three substituents independently selected from R^{21}, R^{22} and R^{23}.

62. A pharmaceutical composition according to claim 61 wherein E is aryl optionally substituted with up to three substituents independently selected from R^{21}, R^{22} and R^{23}.

63. A pharmaceutical composition according to claim 62 wherein E is selected from ArG1 and optionally substituted with up to three substituents independently selected from R^{21}, R^{22} and R^{23}.

64. A pharmaceutical composition according to claim 63 wherein E is phenyl optionally substituted with up to three substituents independently selected from R^{21}, R^{22} and R^{23}.

65. A pharmaceutical composition according to claim 64 wherein the zinc-binding ligand is



66. A pharmaceutical composition according to claim 58 wherein R^{21}, R^{22} and R^{23} are independently selected from

- hydrogen, halogen, $-CHF_2$, $-CF_3$, $-OCF_3$, $-OCHF_2$, $-OCH_2CF_3$, $-OCF_2CHF_2$, $-SCF_3$, $-NO_2$, $-OR^{27}$, $-NR^{27}R^{28}$, $-SR^{27}$, $-C(O)NR^{27}R^{28}$, $-OC(O)NR^{27}R^{28}$, $-NR^{27}C(O)R^{28}$, $-NR^{27}C(O)OR^{28}$, $-CH_2C(O)NR^{27}R^{28}$, $-OCH_2C(O)NR^{27}R^{28}$, $-CH_2OR^{27}$, $-CH_2NR^{27}R^{28}$, $-OC(O)R^{27}$, $-OC_1$-C_6-alkyl-$C(O)OR^{27}$, $-SC_1$-C_6-alkyl-$C(O)OR^{27}$, $-C_2$-C_6-alkenyl-$C(=O)OR^{27}$, $-NR^{27}$-$C(=O)$-C_1-C_6-alkyl-$C(=O)OR^{27}$, $-NR^{27}$-$C(=O)$-C_1-C_6-alkenyl-$C(=O)OR^{27}$-, $-C(=O)NR^{27}$-C_1-C_6-alkyl-$C(=O)OR^{27}$, $-C_1$-C_6-alkyl-$C(=O)OR^{27}$, or $-C(O)OR^{27}$,

- C_1-C_6-alkyl, C_2-C_6-alkenyl or C_2-C_6-alkynyl,

which may optionally be substituted with one or more substituents independently selected from R^{29}

- aryl, aryloxy, aryloxycarbonyl, aroyl, aryl-C_1-C_6-alkoxy, aryl-C_1-C_6-alkyl, aryl-C_2-C_6-alkenyl, aryl-C_2-C_6-alkynyl, heteroaryl, heteroaryl-C_1-C_6-alkyl, heteroaryl-C_2-C_6-alkenyl or heteroaryl-C_2-C_6-alkynyl,

of which the cyclic moieties optionally may be substituted with one or more substituents selected from R^{30}.

67. A pharmaceutical composition according to claim 66 wherein R^{21}, R^{22} and R^{23} are independently selected from

- hydrogen, halogen, $-OCF_3$, $-OR^{27}$, $-NR^{27}R^{28}$, $-SR^{27}$, $-NR^{27}C(O)R^{28}$, $-NR^{27}C(O)OR^{28}$, $-OC(O)R^{27}$, $-OC_1$-C_6-alkyl-$C(O)OR^{27}$, $-SC_1$-C_6-alkyl-$C(O)OR^{27}$, $-C_2$-C_6-alkenyl-

$C(=O)OR^{27}$, $-C(=O)NR^{27}$-C_1-C_6-alkyl-$C(=O)OR^{27}$, $-C_1$-C_6-alkyl-$C(=O)OR^{27}$, or $-C(O)OR^{27}$,

- C_1-C_6-alkyl optionally substituted with one or more substituents independently selected from R^{29}

- aryl, aryloxy, aroyl, aryl-C_1-C_6-alkoxy, aryl-C_1-C_6-alkyl, heteroaryl, heteroaryl-C_1-C_6-alkyl,

of which the cyclic moieties optionally may be substituted with one or more substituents selected from R^{30}.

68. A pharmaceutical composition according to claim 67 wherein R^{21}, R^{22} and R^{23} are independently selected from

- hydrogen, halogen, $-OCF_3$, $-OR^{27}$, $-NR^{27}R^{28}$, $-SR^{27}$, $-NR^{27}C(O)R^{28}$, $-NR^{27}C(O)OR^{28}$, $-OC(O)R^{27}$, $-OC_1$-C_6-alkyl-$C(O)OR^{27}$, $-SC_1$-C_6-alkyl-$C(O)OR^{27}$, $-C_2$-C_6-alkenyl-$C(=O)OR^{27}$, $-C(=O)NR^{27}$-C_1-C_6-alkyl-$C(=O)OR^{27}$, $-C_1$-C_6-alkyl-$C(=O)OR^{27}$, or $-C(O)OR^{27}$,

- methyl, ethyl propyl optionally substituted with one or more substituents independently selected from R^{29}

- aryl, aryloxy, aroyl, aryl-C_1-C_6-alkoxy, aryl-C_1-C_6-alkyl, heteroaryl, heteroaryl-C_1-C_6-alkyl

of which the cyclic moieties optionally may be substituted with one or more substituents selected from R^{30}.

69. A pharmaceutical composition according to claim 68 wherein R^{21}, R^{22} and R^{23} are independently selected from

- hydrogen, halogen, $-OCF_3$, $-OR^{27}$, $-NR^{27}R^{28}$, $-SR^{27}$, $-NR^{27}C(O)R^{28}$, $-NR^{27}C(O)OR^{28}$, $-OC(O)R^{27}$, $-OC_1$-C_6-alkyl-$C(O)OR^{27}$, $-SC_1$-C_6-alkyl-$C(O)OR^{27}$, $-C_2$-C_6-alkenyl-$C(=O)OR^{27}$, $-C(=O)NR^{27}$-C_1-C_6-alkyl-$C(=O)OR^{27}$, $-C_1$-C_6-alkyl-$C(=O)OR^{27}$, or $-C(O)OR^{27}$,

- methyl, ethyl propyl optionally substituted with one or more substituents independently selected from R^{29}

- ArG1, ArG1-O-, ArG1-C(O)-, ArG1-C_1-C_6-alkoxy, ArG1-C_1-C_6-alkyl, Het3, Het3-C_1-C_6-alkyl

of which the cyclic moieties optionally may be substituted with one or more substituents selected from R^{30}.

70. A pharmaceutical composition according to claim 69 wherein R^{21}, R^{22} and R^{23} are independently selected from

- hydrogen, halogen, -OCF_3, -OR^{27}, -$NR^{27}R^{28}$, -SR^{27}, -$NR^{27}C(O)R^{28}$, -$NR^{27}C(O)OR^{28}$, -$OC(O)R^{27}$, -OC_1-C_6-alkyl-$C(O)OR^{27}$, -SC_1-C_6-alkyl-$C(O)OR^{27}$, –C_2-C_6-alkenyl-$C(=O)OR^{27}$, -$C(=O)NR^{27}$-C_1-C_6-alkyl-$C(=O)OR^{27}$, -C_1-C_6-alkyl-$C(=O)OR^{27}$, or -$C(O)OR^{27}$,

- C_1-C_6-alkyl optionally substituted with one or more substituents independently selected from R^{29}

- phenyl, phenyloxy, phenyl-C_1-C_6-alkoxy, phenyl-C_1-C_6-alkyl,

of which the cyclic moieties optionally may be substituted with one or more substituents selected from R^{30}.

71. A pharmaceutical composition according to claim 58 wherein R^{19} is hydrogen or methyl.

72. A pharmaceutical composition according to claim 71 wherein R^{19} is hydrogen.

73. A pharmaceutical composition according to claim 58 wherein R^{27} is Hydrogen, C_1-C_6-alkyl or aryl.

74. A pharmaceutical composition according to claim 73 wherein R^{27} is hydrogen or C_1-C_6-alkyl.

75. A pharmaceutical composition according to claim 58 wherein R^{28} is hydrogen or C_1-C_6-alkyl.

76. A pharmaceutical composition according to claim 58 wherein F is a valence bond.

77. A pharmaceutical composition according to claim 58 wherein F is C_1-C_6-alkylene optionally substituted with one or more hydroxy, C_1-C_6-alkyl, or aryl.

78. A pharmaceutical composition according to claim 58 wherein G is C_1-C_6-alkyl or aryl, wherein the aryl is optionally substituted with up to three substituents R^{24}, R^{25} and R^{26}.

79. A pharmaceutical composition according to claim 58 wherein G is C_1-C_6-alkyl or ArG1, wherein the aryl is optionally substituted with up to three substituents R^{24}, R^{25} and R^{26}.

80. A pharmaceutical composition according to claim 78 wherein G is C_1-C_6-alkyl.

81. A pharmaceutical composition according to claim 80 wherein G is phenyl optionally substituted with up to three substituents R^{24}, R^{25} and R^{26}.

82. A pharmaceutical composition according to claim 58 wherein R^{24}, R^{25} and R^{26} are independently selected from

- hydrogen, halogen, $-CHF_2$, $-CF_3$, $-OCF_3$, $-OCHF_2$, $-OCH_2CF_3$, $-OCF_2CHF_2$, $-SCF_3$, $-NO_2$, $-OR^{27}$, $-NR^{27}R^{28}$, $-SR^{27}$, $-C(O)NR^{27}R^{28}$, $-OC(O)NR^{27}R^{28}$, $-NR^{27}C(O)R^{28}$, $-NR^{27}C(O)OR^{28}$, $-CH_2C(O)NR^{27}R^{28}$, $-OCH_2C(O)NR^{27}R^{28}$, $-CH_2OR^{27}$, $-CH_2NR^{27}R^{28}$, $-OC(O)R^{27}$, $-OC_1$-C_6-alkyl-$C(O)OR^{27}$, $-SC_1$-C_6-alkyl-$C(O)OR^{27}$, $-C_2$-C_6-alkenyl-$C(=O)OR^{27}$, $-NR^{27}$-$C(=O)$-C_1-C_6-alkyl-$C(=O)OR^{27}$, $-NR^{27}$-$C(=O)$-C_1-C_6-alkenyl-$C(=O)OR^{27}$-, $-C(=O)NR^{27}$-C_1-C_6-alkyl-$C(=O)OR^{27}$, $-C_1$-C_6-alkyl-$C(=O)OR^{27}$, or $-C(O)OR^{27}$,

- C_1-C_6-alkyl, C_2-C_6-alkenyl or C_2-C_6-alkynyl,

which may optionally be substituted with one or more substituents independently selected from R^{29}

• aryl, aryloxy, aryloxycarbonyl, aroyl, aryl-C_1-C_6-alkoxy, aryl-C_1-C_6-alkyl, aryl-C_2-C_6-alkenyl, aryl-C_2-C_6-alkynyl, heteroaryl, heteroaryl-C_1-C_6-alkyl, heteroaryl-C_2-C_6-alkenyl or heteroaryl-C_2-C_6-alkynyl,

of which the cyclic moieties optionally may be substituted with one or more substituents selected from R^{30}.

83. A pharmaceutical composition according to claim 82 wherein R^{24}, R^{25} and R^{26} are independently selected from

• hydrogen, halogen, $-OCF_3$, $-OR^{27}$, $-NR^{27}R^{28}$, $-SR^{27}$, $-NR^{27}C(O)R^{28}$, $-NR^{27}C(O)OR^{28}$, $-OC(O)R^{27}$, $-OC_1$-C_6-alkyl-$C(O)OR^{27}$, $-SC_1$-C_6-alkyl-$C(O)OR^{27}$, $-C_2$-C_6-alkenyl-$C(=O)OR^{27}$, $-C(=O)NR^{27}$-C_1-C_6-alkyl-$C(=O)OR^{27}$, $-C_1$-C_6-alkyl-$C(=O)OR^{27}$, or $-C(O)OR^{27}$,

• C_1-C_6-alkyl, C_2-C_6-alkenyl or C_2-C_6-alkynyl,

which may optionally be substituted with one or more substituents independently selected from R^{29}

• aryl, aryloxy, aryloxycarbonyl, aroyl, aryl-C_1-C_6-alkoxy, aryl-C_1-C_6-alkyl, aryl-C_2-C_6-alkenyl, aryl-C_2-C_6-alkynyl, heteroaryl, heteroaryl-C_1-C_6-alkyl, heteroaryl-C_2-C_6-alkenyl or heteroaryl-C_2-C_6-alkynyl,

of which the cyclic moieties optionally may be substituted with one or more substituents selected from R^{30}.

84. A pharmaceutical composition according to claim 83 wherein R^{24}, R^{25} and R^{26} are independently selected from

• hydrogen, halogen, $-OCF_3$, $-OR^{27}$, $-NR^{27}R^{28}$, $-SR^{27}$, $-NR^{27}C(O)R^{28}$, $-NR^{27}C(O)OR^{28}$, $-OC(O)R^{27}$, $-OC_1$-C_6-alkyl-$C(O)OR^{27}$, $-SC_1$-C_6-alkyl-$C(O)OR^{27}$, $-C_2$-C_6-alkenyl-$C(=O)OR^{27}$, $-C(=O)NR^{27}$-C_1-C_6-alkyl-$C(=O)OR^{27}$, $-C_1$-C_6-alkyl-$C(=O)OR^{27}$, or $-C(O)OR^{27}$,

- C_1-C_6-alkyl optionally substituted with one or more substituents independently selected from R^{29}

- aryl, aryloxy, aroyl, aryl-C_1-C_6-alkoxy, aryl-C_1-C_6-alkyl, heteroaryl, heteroaryl-C_1-C_6-alkyl,

of which the cyclic moieties optionally may be substituted with one or more substituents selected from R^{30}.

85. A pharmaceutical composition according to claim 84 wherein R^{21}, R^{22} and R^{23} are independently selected from

- hydrogen, halogen, $-OCF_3$, $-OR^{27}$, $-NR^{27}R^{28}$, $-SR^{27}$, $-NR^{27}C(O)R^{28}$, $-NR^{27}C(O)OR^{28}$, $-OC(O)R^{27}$, $-OC_1$-C_6-alkyl-$C(O)OR^{27}$, $-SC_1$-C_6-alkyl-$C(O)OR^{27}$, $-C_2$-C_6-alkenyl-$C(=O)OR^{27}$, $-C(=O)NR^{27}$-C_1-C_6-alkyl-$C(=O)OR^{27}$, $-C_1$-C_6-alkyl-$C(=O)OR^{27}$, or $-C(O)OR^{27}$,

- methyl, ethyl propyl optionally substituted with one or more substituents independently selected from R^{29}

- ArG1, ArG1-O-, ArG1-C(O)-, ArG1-C_1-C_6-alkoxy, ArG1-C_1-C_6-alkyl, Het3, Het3-C_1-C_6-alkyl

of which the cyclic moieties optionally may be substituted with one or more substituents selected from R^{30}.

86. A pharmaceutical composition according to claim 85 wherein R^{21}, R^{22} and R^{23} are independently selected from

- hydrogen, halogen, $-OCF_3$, $-OR^{27}$, $-NR^{27}R^{28}$, $-SR^{27}$, $-NR^{27}C(O)R^{28}$, $-NR^{27}C(O)OR^{28}$, $-OC(O)R^{27}$, $-OC_1$-C_6-alkyl-$C(O)OR^{27}$, $-SC_1$-C_6-alkyl-$C(O)OR^{27}$, $-C_2$-C_6-alkenyl-$C(=O)OR^{27}$, $-C(=O)NR^{27}$-C_1-C_6-alkyl-$C(=O)OR^{27}$, $-C_1$-C_6-alkyl-$C(=O)OR^{27}$, or $-C(O)OR^{27}$,

- methyl, ethyl propyl optionally substituted with one or more substituents independently selected from R^{29}

- ArG1, ArG1-O-, ArG1-C(O)-, ArG1-C_1-C_6-alkoxy, ArG1-C_1-C_6-alkyl, Het3, Het3-C_1-C_6-alkyl

of which the cyclic moieties optionally may be substituted with one or more substituents selected from R^{30}.

87. A pharmaceutical composition according to claim 86 wherein R^{21}, R^{22} and R^{23} are independently selected from

- hydrogen, halogen, $-OCF_3$, $-OR^{27}$, $-NR^{27}R^{28}$, $-SR^{27}$, $-NR^{27}C(O)R^{28}$, $-NR^{27}C(O)OR^{28}$, $-OC(O)R^{27}$, $-OC_1$-C_6-alkyl-$C(O)OR^{27}$, $-SC_1$-C_6-alkyl-$C(O)OR^{27}$, $-C_2$-C_6-alkenyl-$C(=O)OR^{27}$, $-C(=O)NR^{27}$-C_1-C_6-alkyl-$C(=O)OR^{27}$, $-C_1$-C_6-alkyl-$C(=O)OR^{27}$, or $-C(O)OR^{27}$,
- methyl, ethyl propyl optionally substituted with one or more substituents independently selected from R^{29}

- ArG1, ArG1-O-, ArG1-C_1-C_6-alkoxy, ArG1-C_1-C_6-alkyl,

of which the cyclic moieties optionally may be substituted with one or more substituents selected from R^{30}.

88. A pharmaceutical composition according to claim 58 wherein R^{20} is hydrogen or methyl.

89. A pharmaceutical composition according to claim 88 wherein R^{20} is hydrogen.

90. A pharmaceutical composition according to claim 58 wherein R^{27} is hydrogen, C_1-C_6-alkyl or aryl.

91. A pharmaceutical composition according to claim 90 wherein R^{27} is hydrogen or C_1-C_6-alkyl or ArG1.

92. A pharmaceutical composition according to claim 91 wherein R^{27} is hydrogen or C_1-C_6-alkyl.

93. A pharmaceutical composition according to claim 58 wherein R^{28} is hydrogen or C_1-C_6-alkyl.

94. A pharmaceutical composition according to claim 58 wherein R^{17} and R^{18} are independently selected from

- hydrogen, halogen, -CN, $-CF_3$, $-OCF_3$, $-NO_2$, $-OR^{27}$, $-NR^{27}R^{28}$, $-SR^{27}$, $-S(O)R^{27}$, $-S(O)_2R^{27}$, $-C(O)NR^{27}R^{28}$, $-CH_2OR^{27}$, $-OC(O)R^{27}$, $-OC_1$-C_6-alkyl-$C(O)OR^{27}$, $-SC_1$-C_6-alkyl-$C(O)OR^{27}$, or $-C(O)OR^{27}$,

- C_1-C_6-alkyl, C_2-C_6-alkenyl or C_2-C_6-alkynyl, optionally substituted with one or more substituents independently selected from R^{29}

- aryl, aryloxy, aroyl, aryl-C_1-C_6-alkoxy, aryl-C_1-C_6-alkyl, heteroaryl, heteroaryl-C_1-C_6-alkyl,

of which the cyclic moieties optionally may be substituted with one or more substituents selected from R^{30}.

95. A pharmaceutical composition according to claim 94 wherein R^{17} and R^{18} are independently selected from

- hydrogen, halogen, -CN, $-CF_3$, $-NO_2$, $-OR^{27}$, $-NR^{27}R^{28}$, or $-C(O)OR^{27}$,

- C_1-C_6-alkyl optionally substituted with one or more substituents independently selected from R^{29}

- aryl, aryloxy, aroyl, aryl-C_1-C_6-alkoxy, aryl-C_1-C_6-alkyl, heteroaryl, heteroaryl-C_1-C_6-alkyl,

of which the cyclic moieties optionally may be substituted with one or more substituents selected from R^{30}.

96. A pharmaceutical composition according to claim 95 wherein R^{17} and R^{18} are independently selected from

- hydrogen, halogen, -CN, $-CF_3$, $-NO_2$, $-OR^{27}$, $-NR^{27}R^{28}$, or $-C(O)OR^{27}$
- methyl, ethyl propyl optionally substituted with one or more substituents independently selected from R^{29}

- aryl, aryloxy, aroyl, aryl-C_1-C_6-alkoxy, aryl-C_1-C_6-alkyl, heteroaryl, heteroaryl-C_1-C_6-alkyl

of which the cyclic moieties optionally may be substituted with one or more substituents selected from R^{30}.

97. A pharmaceutical composition according to claim 96 wherein R^{17} and R^{18} are independently selected from

- hydrogen, halogen, -CN, -CF_3, -NO_2, -OR^{27}, -$NR^{27}R^{28}$, or -$C(O)OR^{27}$
- methyl, ethyl propyl optionally substituted with one or more substituents independently selected from R^{29}
- ArG1, ArG1-O-, ArG1-C(O)-, ArG1-C_1-C_6-alkoxy, ArG1-C_1-C_6-alkyl, Het3, Het3-C_1-C_6-alkyl

of which the cyclic moieties optionally may be substituted with one or more substituents selected from R^{30}.

98. A pharmaceutical composition according to claim 97 wherein R^{17} and R^{18} are independently selected from

- hydrogen, halogen, -CN, -CF_3, -NO_2, -OR^{27}, -$NR^{27}R^{28}$, or -$C(O)OR^{27}$
- C_1-C_6-alkyl optionally substituted with one or more substituents independently selected from R^{29}
- phenyl, phenyloxy, phenyl-C_1-C_6-alkoxy, phenyl-C_1-C_6-alkyl,

of which the cyclic moieties optionally may be substituted with one or more substituents selected from R^{30}.

99. A pharmaceutical composition according to claim 58 wherein R^{27} is hydrogen or C_1-C_6-alkyl.

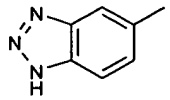
100. A pharmaceutical composition according to claim 99 wherein R^{27} is hydrogen, methyl or ethyl.

101. A pharmaceutical composition according to claim 58 wherein R^{28} is hydrogen or C_1-C_6-alkyl.

102. A pharmaceutical composition according to claim 101 wherein R^{28} is hydrogen, methyl or ethyl.

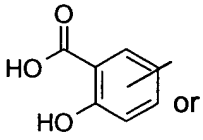
103. A pharmaceutical composition according to claim 58 wherein R^{72} is –OH or phenyl.

104. A pharmaceutical composition according to claim 58 wherein the zinc-binding ligand is



105. A pharmaceutical composition according to claim 1 wherein the zinc-binding ligand is of the form H-I-J

wherein H is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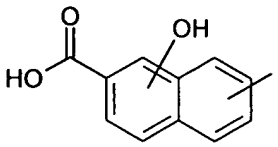
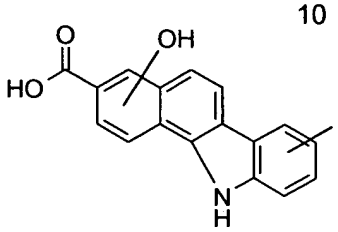
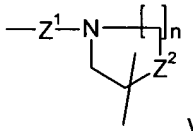

or


wherein the phenyl, naphthalene or benzocarbazole rings are optionally substituted with one or more substituents independently selected from R^{31}

I is selected from

- a valence bond,
- $–CH_2N(R^{32})-$ or $–SO_2N(R^{33})-$,
-  wherein Z^1 is $S(O)_2$ or CH_2, Z^2 is -NH-, -O-or -S-, and n is 1 or 2,

J is

- C_1-C_6-alkyl, C_2-C_6-alkenyl or C_2-C_6-alkynyl, which may each optionally be substituted with one or more substituents selected from R^{34},
- Aryl, aryloxy, aryl-oxycarbonyl-, aroyl, aryl-C_1-C_6-alkoxy-, aryl-C_1-C_6-alkyl-, aryl-C_2-C_6-alkenyl-, aryl-C_2-C_6-alkynyl-, heteroaryl, heteroaryl-C_1-C_6-alkyl-, heteroaryl-C_2-C_6-alkenyl- or heteroaryl-C_2-C_6-alkynyl-, wherein the cyclic moieties are optionally substituted with one or more substituents selected from R^{37},

• Hydrogen,

R^{31} is independently selected from hydrogen, halogen, -CN, $-CH_2CN$, $-CHF_2$, $-CF_3$, $-OCF_3$, $-OCHF_2$, $-OCH_2CF_3$, $-OCF_2CHF_2$, $-S(O)_2CF_3$, $-SCF_3$, $-NO_2$, $-OR^{35}$, $-C(O)R^{35}$, $-NR^{35}R^{36}$, $-SR^{35}$, $-NR^{35}S(O)_2R^{36}$, $-S(O)_2NR^{35}R^{36}$, $-S(O)NR^{35}R^{36}$, $-S(O)R^{35}$, $-S(O)_2R^{35}$, $-C(O)NR^{35}R^{36}$, $-OC(O)NR^{35}R^{36}$, $-NR^{35}C(O)R^{36}$, $-CH_2C(O)NR^{35}R^{36}$, $-OCH_2C(O)NR^{35}R^{36}$, $-CH_2OR^{35}$, $-CH_2NR^{35}R^{36}$, $-OC(O)R^{35}$, $-OC_1$-C_6-alkyl-$C(O)OR^{35}$, $-SC_1$-C_6-alkyl-$C(O)OR^{35}$ $-C_2$-C_6-alkenyl-$C(=O)OR^{35}$, $-NR^{35}$-$C(=O)$-C_1-C_6-alkyl-$C(=O)OR^{35}$, $-NR^{35}$-$C(=O)$-C_1-C_6-alkenyl-$C(=O)OR^{35}$-, C_1-C_6-alkyl, C_1-C_6-alkanoyl or $-C(O)OR^{35}$,

R^{32} and R^{33} are independently selected from hydrogen, C_1-C_6-alkyl or C_1-C_6-alkanoyl,

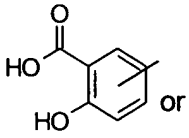
R^{34} is independently selected from halogen, -CN, $-CF_3$, $-OCF_3$, $-OR^{35}$, and $-NR^{35}R^{36}$,

R^{35} and R^{36} are independently selected from hydrogen, C_1-C_6-alkyl, aryl-C_1-C_6-alkyl or aryl, or R^{35} and R^{36} when attached to the same nitrogen atom together with the said nitrogen atom may form a 3 to 8 membered heterocyclic ring optionally containing one or two further heteroatoms selected from nitrogen, oxygen and sulphur, and optionally containing one or two double bonds,

R^{37} is independently selected from halogen, $-C(O)OR^{35}$, -C(O)H, -CN, $-CF_3$, $-OCF_3$, $-NO_2$, $-OR^{35}$, $-NR^{35}R^{36}$, C_1-C_6-alkyl or C_1-C_6-alkanoyl,

or any enantiomer, diastereomer, racemic mixture, tautomer, or salt thereof with a pharmaceutically acceptable acid or base.

106. A pharmaceutical composition according to claim 105 wherein the zinc-binding ligand is of the form H-I-J, wherein H is



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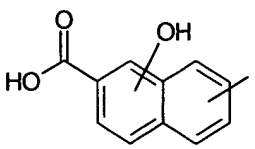
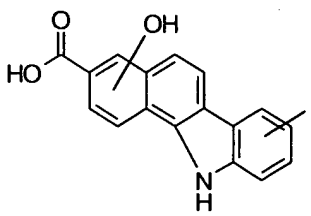
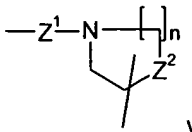


or


wherein the phenyl, naphthalene or benzocarbazole rings are optionally substituted with one or more substituents independently selected from R^{31},

I is selected from

- a valence bond,
- $-CH_2N(R^{32})-$ or $-SO_2N(R^{33})-$,
-  wherein Z^1 is $S(O)_2$ or CH_2, Z^2 is N,-O-or -S-, and n is 1 or 2,

J is

- C_1-C_6-alkyl, C_2-C_6-alkenyl or C_2-C_6-alkynyl, which may each optionally be substituted with one or more substituents selected from R^{34},
- Aryl, aryloxy, aryl-oxycarbonyl-, aroyl, aryl-C_1-C_6-alkoxy-, aryl-C_1-C_6-alkyl-, aryl-C_2-C_6-alkenyl-, aryl-C_2-C_6-alkynyl-, heteroaryl, heteroaryl-C_1-C_6-alkyl-, heteroaryl-C_2-C_6-alkenyl- or heteroaryl-C_2-C_6-alkynyl-, wherein the cyclic moieties are optionally substituted with one or more substituents selected from R^{37},
- hydrogen,

R^{31} is independently selected from hydrogen, halogen, -CN, $-CH_2CN$, $-CHF_2$, $-CF_3$, $-OCF_3$, $-OCHF_2$, $-OCH_2CF_3$, $-OCF_2CHF_2$, $-S(O)_2CF_3$, $-SCF_3$, $-NO_2$, $-OR^{35}$, $-C(O)R^{35}$, $-NR^{35}R^{36}$, $-SR^{35}$, $-NR^{35}S(O)_2R^{36}$, $-S(O)_2NR^{35}R^{36}$, $-S(O)NR^{35}R^{36}$, $-S(O)R^{35}$, $-S(O)_2R^{35}$, $-C(O)NR^{35}R^{36}$, $-OC(O)NR^{35}R^{36}$, $-NR^{35}C(O)R^{36}$, $-CH_2C(O)NR^{35}R^{36}$, $-OCH_2C(O)NR^{35}R^{36}$, $-CH_2OR^{35}$, $-CH_2NR^{35}R^{36}$, $-OC(O)R^{35}$, $-OC_1$-C_6-alkyl-$C(O)OR^{35}$, $-SC_1$-C_6-alkyl-$C(O)OR^{35}$ $-C_2$-C_6-alkenyl-$C(=O)OR^{35}$, $-NR^{35}$-$C(=O)$-C_1-C_6-alkyl-$C(=O)OR^{35}$, $-NR^{35}$-$C(=O)$-C_1-C_6-alkenyl-$C(=O)OR^{35}$-, C_1-C_6-alkyl, C_1-C_6-alkanoyl or $-C(O)OR^{35}$,

R^{32} and R^{33} are independently selected from hydrogen, C_1-C_6-alkyl or C_1-C_6-alkanoyl,

R^{34} is independently selected from halogen, -CN, $-CF_3$, $-OCF_3$, $-OR^{35}$, and $-NR^{35}R^{36}$,

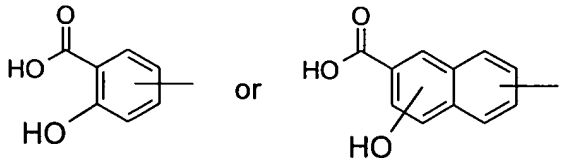
R^{35} and R^{36} are independently selected from hydrogen, C_1-C_6-alkyl, aryl-C_1-C_6-alkyl or aryl, or R^{35} and R^{36} when attached to the same nitrogen atom together with the nitrogen atom may form a 3 to 8 membered heterocyclic ring optionally containing one or two further heteroatoms selected from nitrogen, oxygen and sulphur, and optionally containing one or two double bonds,

R^{37} is independently selected from halogen, -C(O)OR^{35}, -C(O)H, -CN, -CF_3, -OCF_3, -NO_2, -OR^{35}, -$NR^{35}R^{36}$, C_1-C_6-alkyl or C_1-C_6-alkanoyl,

or any enantiomer, diastereomer, racemic mixture, tautomer, or salt thereof with a pharmaceutically acceptable acid or base,

with the proviso that R^{31} and J cannot both be hydrogen.

107. A pharmaceutical composition according to claim 105 wherein H is



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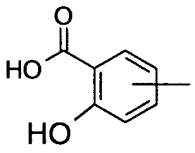
108. A pharmaceutical composition according to claim 107 wherein H is



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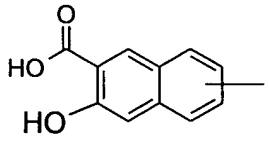
109. A pharmaceutical composition according to claim 107 wherein H is



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110. A pharmaceutical composition according to claim 105 wherein I is a valence bond, –$CH_2N(R^{32})$-, or –$SO_2N(R^{33})$-.

111. A pharmaceutical composition according to claim 110 wherein I is a valence bond.

112. A pharmaceutical composition according to claim 105 wherein J is

- hydrogen,
- C_1-C_6-alkyl, C_2-C_6-alkenyl or C_2-C_6-alkynyl,

which may optionally be substituted with one or more substituents selected from halogen, -CN, $-CF_3$, $-OCF_3$, $-OR^{35}$, and $-NR^{35}R^{36}$,

- aryl, or heteroaryl, wherein the cyclic moieties are optionally substituted with one or more substituents independently selected from R^{37}.
-

113. A pharmaceutical composition according to claim 112 wherein J is

- hydrogen,
- aryl or heteroaryl, wherein the cyclic moieties are optionally substituted with one or more substituents independently selected from R^{37}.
-

114. A pharmaceutical composition according to claim 112 wherein J is

- hydrogen,
- ArG1 or Het3, wherein the cyclic moieties are optionally substituted with one or more substituents independently selected from R^{37}.
-

115. A pharmaceutical composition according to claim 114 wherein J is

- hydrogen,
- phenyl or naphthyl optionally substituted with one or more substituents independently selected from R^{37}.
-

116. A pharmaceutical composition according to claim 115 wherein J is hydrogen.

117. A pharmaceutical composition according to claim 105 wherein R^{32} and R^{33} are independently selected from hydrogen or C_1-C_6-alkyl.

118. A pharmaceutical composition according to claim 105 wherein R^{34} is hydrogen, halogen, -CN, $-CF_3$, $-OCF_3$, $-SCF_3$, $-NO_2$, $-OR^{35}$, $-C(O)R^{35}$, $-NR^{35}R^{36}$, $-SR^{35}$, $-C(O)NR^{35}R^{36}$, $-OC(O)NR^{35}R^{36}$, $-NR^{35}C(O)R^{36}$, $-OC(O)R^{35}$, $-OC_1$-C_6-alkyl-$C(O)OR^{35}$, $-SC_1$-C_6-alkyl-$C(O)OR^{35}$ or $-C(O)OR^{35}$.

119. A pharmaceutical composition according to claim 118 wherein R^{34} is hydrogen, halogen, $-CF_3$, $-NO_2$, $-OR^{35}$, $-NR^{35}R^{36}$, $-SR^{35}$, $-NR^{35}C(O)R^{36}$, or $-C(O)OR^{35}$.

120. A pharmaceutical composition according to claim 119 wherein R^{34} is hydrogen, halogen, $-CF_3$, $-NO_2$, $-OR^{35}$, $-NR^{35}R^{36}$, or $-NR^{35}C(O)R^{36}$.

121. A pharmaceutical composition according to claim 120 wherein R^{34} is hydrogen, halogen, or $-OR^{35}$.

122. A pharmaceutical composition according to claim 105 wherein R^{35} and R^{36} are independently selected from hydrogen, C_1-C_6-alkyl, or aryl.

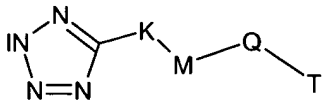
123. A pharmaceutical composition according to claim 122 wherein R^{35} and R^{36} are independently selected from hydrogen or C_1-C_6-alkyl.

124. A pharmaceutical composition according to claim 105 wherein R^{37} is halogen, $-C(O)OR^{35}$, -CN, $-CF_3$, $-OR^{35}$, $-NR^{35}R^{36}$, C_1-C_6-alkyl or C_1-C_6-alkanoyl.

125. A pharmaceutical composition according to claim 124 wherein R^{37} is halogen, $-C(O)OR^{35}$, $-OR^{35}$, $-NR^{35}R^{36}$, C_1-C_6-alkyl or C_1-C_6-alkanoyl.

126. A pharmaceutical composition according to claim 125 wherein R^{37} is halogen, $-C(O)OR^{35}$ or $-OR^{35}$.

127. A pharmaceutical composition according to claim 1 wherein the zinc-binding ligand is



wherein K is a valence bond, C_1-C_6-alkylene, -NH-C(=O)-U-, $-C_1$-C_6-alkyl-S-, $-C_1$-C_6-alkyl-O-, -C(=O)-, or -C(=O)-NH-, wherein any C_1-C_6-alkyl moiety is optionally substituted with R^{38},

U is a valence bond, C_1-C_6-alkenylene, $-C_1$-C_6-alkyl-O- or C_1-C_6-alkylene wherein any C_1-C_6-alkyl moiety is optionally substituted with C_1-C_6-alkyl,

R^{38} is C_1-C_6-alkyl, aryl, wherein the alkyl or aryl moieties are optionally substituted with one or more substituents independently selected from R^{39},

R^{39} is independently selected from halogen, cyano, nitro, amino,

M is a valence bond, arylene or heteroarylene, wherein the aryl or heteroaryl moieties are optionally substituted with one or more substituents independently selected from R^{40},

R^{40} is selected from

- hydrogen, halogen, -CN, $-CH_2CN$, $-CHF_2$, $-CF_3$, $-OCF_3$, $-OCHF_2$, $-OCH_2CF_3$, $-OCF_2CHF_2$, $-S(O)_2CF_3$, $-OS(O)_2CF_3$, $-SCF_3$, $-NO_2$, $-OR^{41}$, $-NR^{41}R^{42}$, $-SR^{41}$, $-NR^{41}S(O)_2R^{42}$, $-S(O)_2NR^{41}R^{42}$, $-S(O)NR^{41}R^{42}$, $-S(O)R^{41}$, $-S(O)_2R^{41}$, $-OS(O)_2\ R^{41}$, $-C(O)NR^{41}R^{42}$, $-OC(O)NR^{41}R^{42}$, $-NR^{41}C(O)R^{42}$, $-CH_2C(O)NR^{41}R^{42}$, $-OC_1$-C_6-alkyl-$C(O)NR^{41}R^{42}$, $-CH_2OR^{41}$, $-CH_2OC(O)R^{41}$, $-CH_2NR^{41}R^{42}$, $-OC(O)R^{41}$, $-OC_1$-C_6-alkyl-$C(O)OR^{41}$, $-OC_1$-C_6-alkyl-OR^{41}, -S-C_1-C_6-alkyl-$C(O)OR^{41}$, $-C_2$-C_6-alkenyl-$C(=O)OR^{41}$, $-NR^{41}$-$C(=O)$-C_1-C_6-alkyl-$C(=O)OR^{41}$, $-NR^{41}$-$C(=O)$-C_1-C_6-alkenyl-$C(=O)OR^{41}$, $-C(O)OR^{41}$, $-C_2$-C_6-alkenyl-$C(=O)R^{41}$, =O, -NH-$C(=O)$-O-C_1-C_6-alkyl, or -NH-$C(=O)$-$C(=O)$-O-C_1-C_6-alkyl,

- C_1-C_6-alkyl, C_2-C_6-alkenyl or C_2-C_6-alkynyl, which may each optionally be substituted with one or more substituents selected from R^{43},

- aryl, aryloxy, aryloxycarbonyl, aroyl, arylsulfanyl, aryl-C_1-C_6-alkoxy, aryl-C_1-C_6-alkyl, aryl-C_2-C_6-alkenyl, aroyl-C_2-C_6-alkenyl, aryl-C_2-C_6-alkynyl, heteroaryl, heteroaryl-C_1-C_6-alkyl, heteroaryl-C_2-C_6-alkenyl or heteroaryl-C_2-C_6-alkynyl, wherein the cyclic moieties optionally may be substituted with one or more substituents selected from R^{44},

R^{41} and R^{42} are independently selected from hydrogen, -OH, C_1-C_6-alkyl, C_1-C_6-alkenyl, aryl-C_1-C_6-alkyl or aryl, wherein the alkyl moieties may optionally be substituted with one or more substituents independently selected from R^{45}, and the aryl moieties may optionally be substituted with one or more substituents independently selected from R^{46}; R^{41} and R^{42} when attached to the same nitrogen atom may form a 3 to 8 membered heterocyclic ring with the said nitrogen atom, the heterocyclic ring optionally containing one or two further heteroatoms

selected from nitrogen, oxygen and sulphur, and optionally containing one or two double bonds,

R^{43} is independently selected from halogen, -CN, $-CF_3$, $-OCF_3$, $-OR^{41}$, and $-NR^{41}R^{42}$

R^{44} is independently selected from halogen, $-C(O)OR^{41}$, $-CH_2C(O)OR^{41}$, $-CH_2OR^{41}$, -CN, $-CF_3$, $-OCF_3$, $-NO_2$, $-OR^{41}$, $-NR^{41}R^{42}$ and C_1-C_6-alkyl,

R^{45} is independently selected from halogen, -CN, $-CF_3$, $-OCF_3$, -O-C_1-C_6-alkyl, -C(O)-O-C_1-C_6-alkyl, -COOH and $-NH_2$,

R^{46} is independently selected from halogen, $-C(O)OC_1$-C_6-alkyl, -COOH, -CN, $-CF_3$, $-OCF_3$, $-NO_2$, -OH, $-OC_1$-C_6-alkyl, $-NH_2$, C(=O) or C_1-C_6-alkyl,

Q is a valence bond, C_1-C_6-alkylene, -C_1-C_6-alkyl-O-, -C_1-C_6-alkyl-NH-, -NH-C_1-C_6-alkyl, -NH-C(=O)-, -C(=O)-NH-, -O-C_1-C_6-alkyl, -C(=O)-, or -C_1-C_6-alkyl-C(=O)-N(R^{47})- wherein the alkyl moieties are optionally substituted with one or more substituents independently selected from R^{48},

R^{47} and R^{48} are independently selected from hydrogen, C_1-C_6-alkyl, aryl optionally substituted with one or more R^{49},

R^{49} is independently selected from halogen and –COOH,

T is

- hydrogen,
- C_1-C_6-alkyl, C_2-C_6-alkenyl , C_2-C_6-alkynyl, C_1-C_6-alkyloxy-carbonyl, wherein the alkyl, alkenyl and alkynyl moieties are optionally substituted with one or more substituents independently selected from R^{50},
- aryl, aryloxy, aryloxy-carbonyl, aryl-C_1-C_6-alkyl, aroyl, aryl-C_1-C_6-alkoxy, aryl-C_2-C_6-alkenyl, aryl-C_2-C_6-alkyny-, heteroaryl, heteroaryl-C_1-C_6-alkyl, heteroaryl-C_2-C_6-alkenyl, heteroaryl-C_2-C_6-alkynyl,

wherein any alkyl, alkenyl , alkynyl, aryl and heteroaryl moiety is optionally substituted with one or more substituents independently selected from R^{50},

R^{50} is C_1-C_6-alkyl, C_1-C_6-alkoxy, aryl, aryloxy, aryl-C_1-C_6-alkoxy, -C(=O)-NH-C_1-C_6-alkyl-aryl, -C(=O)-NR^{50A}-C_1-C_6-alkyl, -C(=O)-NH-$(CH_2CH_2O)_mC_1$-C_6-alkyl-COOH, heteroaryl, heteroaryl-C_1-C_6-alkoxy, -C_1-C_6-alkyl-COOH, -O-C_1-C_6-alkyl-COOH, -$S(O)_2R^{51}$, -C_2-C_6-alkenyl-COOH, -OR^{51}, -NO_2, halogen, -COOH, -CF_3, -CN, =O, -$N(R^{51}R^{52})$, wherein m is 1, 2, 3 or 4, and wherein the aryl or heteroaryl moieties are optionally substituted with one or more R^{53}, and the alkyl moieties are optionally substituted with one or more R^{50B}.

R^{50A} and R^{50B} are independently selected from -C(O)OC_1-C_6-alkyl, -COOH, -C_1-C_6-alkyl-C(O)OC_1-C_6-alkyl, -C_1-C_6-alkyl-COOH, or C_1-C_6-alkyl,

R^{51} and R^{52} are independently selected from hydrogen and C_1-C_6-alkyl,

R^{53} is independently selected from C_1-C_6-alkyl, C_1-C_6-alkoxy, -C_1-C_6-alkyl-COOH, -C_2-C_6-alkenyl-COOH, -OR^{51}, -NO_2, halogen, -COOH, -CF_3, -CN, or -$N(R^{51}R^{52})$,

or any enantiomer, diastereomer, racemic mixture, tautomer, or salt thereof with a pharmaceutically acceptable acid or base.

128. A pharmaceutical composition according to claim 127 wherein K is a valence bond, C_1-C_6-alkylene, -NH-C(=O)-U-, -C_1-C_6-alkyl-S-, -C_1-C_6-alkyl-O-, or -C(=O)-, wherein any C_1-C_6-alkyl moiety is optionally substituted with R^{38}.

129. A pharmaceutical composition according to claim 128 wherein K is a valence bond, C_1-C_6-alkylene, -NH-C(=O)-U-, -C_1-C_6-alkyl-S-, or -C_1-C_6-alkyl-O, wherein any C_1-C_6-alkyl moiety is optionally substituted with R^{38}.

130. A pharmaceutical composition according to claim 129 wherein K is a valence bond, C_1-C_6-alkylene, or -NH-C(=O)-U, wherein any C_1-C_6-alkyl moiety is optionally substituted with R^{38}.

131. A pharmaceutical composition according to claim 130 wherein K is a valence bond or C_1-C_6-alkylene, wherein any C_1-C_6-alkyl moiety is optionally substituted with R^{38}.

132. A pharmaceutical composition according to claim 130 wherein K is a valence bond or -NH-C(=O)-U.

133. A pharmaceutical composition according to claim 131 wherein K is a valence bond.

134. A pharmaceutical composition according to claim 127 wherein U is a valence bond or -C_1-C_6-alkyl-O-.

135. A pharmaceutical composition according to claim 134 wherein U is a valence bond.

136. A pharmaceutical composition according to claim 127 wherein M is arylene or heteroarylene, wherein the arylene or heteroarylene moieties are optionally substituted with one or more substituents independently selected from R^{40}.

137. A pharmaceutical composition according to claim 136 wherein M is ArG1 or Het1, wherein the arylene or heteroarylene moieties are optionally substituted with one or more substituents independently selected from R^{40}.

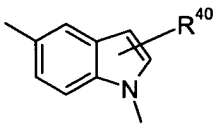
138. A pharmaceutical composition according to claim 137 wherein M is ArG1 or Het2, wherein the arylene or heteroarylene moieties are optionally substituted with one or more substituents independently selected from R^{40}.

139. A pharmaceutical composition according to claim 138 wherein M is ArG1 or Het3, wherein the arylene or heteroarylene moieties are optionally substituted with one or more substituents independently selected from R^{40}.

140. A pharmaceutical composition according to claim 139 wherein M is phenylene optionally substituted with one or more substituents independently selected from R^{40}.

141. A pharmaceutical composition according to claim 139 wherein M is indolylene optionally substituted with one or more substituents independently selected from R^{40}.

142. A pharmaceutical composition according to claim 141 wherein M is



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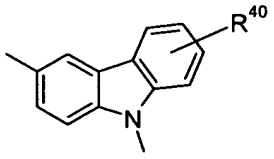
143. A pharmaceutical composition according to claim 139 wherein M is carbazolylene optionally substituted with one or more substituents independently selected from R^{40}.

144. A pharmaceutical composition according to claim 143 wherein M is



145. A pharmaceutical composition according to claim 127 wherein R^{40} is selected from

- hydrogen, halogen, -CN, $-CF_3$, $-OCF_3$, $-NO_2$, $-OR^{41}$, $-NR^{41}R^{42}$, $-SR^{41}$, $-S(O)_2R^{41}$, $-NR^{41}C(O)R^{42}$, $-OC_1$-C_6-alkyl-$C(O)NR^{41}R^{42}$, $-C_2$-C_6-alkenyl-$C(=O)OR^{41}$, $-C(O)OR^{41}$, =O, -NH-C(=O)-O-C_1-C_6-alkyl, or -NH-C(=O)-C(=O)-O-C_1-C_6-alkyl,

C_1-C_6-alkyl or C_2-C_6- alkenyl which may each optionally be substituted with one or more substituents independently selected from R^{43},

- aryl, aryloxy, aryl-C_1-C_6-alkoxy, aryl-C_1-C_6-alkyl, aryl-C_2-C_6-alkenyl, heteroaryl, heteroaryl-C_1-C_6-alkyl, or heteroaryl-C_2-C_6-alkenyl, wherein the cyclic moieties optionally may be substituted with one or more substituents selected from R^{44}.
-

146. A pharmaceutical composition according to claim 145 wherein R^{40} is selected from

- hydrogen, halogen, -CN, $-CF_3$, $-OCF_3$, $-NO_2$, $-OR^{41}$, $-NR^{41}R^{42}$, $-SR^{41}$, $-S(O)_2R^{41}$, $-NR^{41}C(O)R^{42}$, $-OC_1$-C_6-alkyl-$C(O)NR^{41}R^{42}$, $-C_2$-C_6-alkenyl-$C(=O)OR^{41}$, $-C(O)OR^{41}$, =O, -NH-C(=O)-O-C_1-C_6-alkyl, or -NH-C(=O)-C(=O)-O-C_1-C_6-alkyl,

C_1-C_6-alkyl or C_2-C_6- alkenyl which may each optionally be substituted with one or more substituents independently selected from R^{43},

- ArG1, ArG1-O-, ArG1-C_1-C_6-alkoxy, ArG1-C_1-C_6-alkyl, ArG1-C_2-C_6-alkenyl, Het3, Het3-C_1-C_6-alkyl, or Het3-C_2-C_6-alkenyl, wherein the cyclic moieties optionally may be substituted with one or more substituents selected from R^{44}.

147. A pharmaceutical composition according to claim 146 wherein R^{40} is selected from

- hydrogen, halogen, $-CF_3$, $-NO_2$, $-OR^{41}$, $-NR^{41}R^{42}$, $-C(O)OR^{41}$, =O, or $-NR^{41}C(O)R^{42}$,
- C_1-C_6-alkyl, and
- ArG1.

148. A pharmaceutical composition according to claim 147 wherein R^{40} is hydrogen.

149. A pharmaceutical composition according to claim 147 wherein R^{40} is selected from

- Halogen, $-NO_2$, $-OR^{41}$, $-NR^{41}R^{42}$, $-C(O)OR^{41}$, or $-NR^{41}C(O)R^{42}$,
- Methyl, and
- Phenyl.

150. A pharmaceutical composition according to claim 127 wherein R^{41} and R^{42} are independently selected from hydrogen, C_1-C_6-alkyl, or aryl, wherein the aryl moieties may optionally be substituted with halogen or –COOH.

151. A pharmaceutical composition according to claim 150 wherein R^{41} and R^{42} are independently selected from hydrogen, methyl, ethyl, or phenyl, wherein the phenyl moieties may optionally be substituted with halogen or –COOH.

152. A pharmaceutical composition according to claim 127 wherein Q is a valence bond, C_1-C_6-alkylene, -C_1-C_6-alkyl-O-, -C_1-C_6-alkyl-NH-, -NH-C_1-C_6-alkyl, -NH-C(=O)-, -C(=O)-NH-, -O-C_1-C_6-alkyl, -C(=O)-, or -C_1-C_6-alkyl-C(=O)-N(R^{47})- wherein the alkyl moieties are optionally substituted with one or more substituents independently selected from R^{48}.

153. A pharmaceutical composition according to claim 152 wherein Q is a valence bond, $-CH_2-$, $-CH_2-CH_2-$, $-CH_2-O-$, $-CH_2-CH_2-O-$, $-CH_2-NH-$, $-CH_2-CH_2-NH-$, $-NH-CH_2-$, $-NH-CH_2-CH_2-$, -NH-C(=O)-, -C(=O)-NH-, $-O-CH_2-$, $-O-CH_2-CH_2-$, or -C(=O)-.

154. A pharmaceutical composition according to claim 127 wherein R^{47} and R^{48} are independently selected from hydrogen, methyl and phenyl.

155. A pharmaceutical composition according to claim 127 wherein T is

- Hydrogen,
- C_1-C_6-alkyl optionally substituted with one or more substituents independently selected from R^{50},
- aryl, aryl-C_1-C_6-alkyl, heteroaryl, wherein the alkyl, aryl and heteroaryl moieties are optionally substituted with one or more substituents independently selected from R^{50}.
-

156. A pharmaceutical composition according to claim 155 wherein T is

- hydrogen,
- C_1-C_6-alkyl optionally substituted with one or more substituents independently selected from R^{50},
- ArG1, ArG1-C_1-C_6-alkyl, Het3, wherein the alkyl, aryl and heteroaryl moieties are optionally substituted with one or more substituents independently selected from R^{50}.

157. A pharmaceutical composition according to claim 156 wherein T is

- hydrogen,
- C_1-C_6-alkyl, optionally substituted with one or more substituents independently selected from R^{50},
- phenyl, phenyl-C_1-C_6-alkyl, wherein the alkyl and phenyl moieties are optionally substituted with one or more substituents independently selected from R^{50}.
-

158. A pharmaceutical composition according to claim 157 wherein T is phenyl substituted with R^{50}.

159. A pharmaceutical composition according to claim 127 wherein R^{50} is C_1-C_6-alkyl, C_1-C_6-alkoxy, aryl, aryloxy, aryl-C_1-C_6-alkoxy, -C(=O)-NH-C_1-C_6-alkyl-aryl, -C(=O)-NR^{50A}-C_1-C_6-alkyl, -C(=O)-NH-$(CH_2CH_2O)_m$$C_1$-$C_6$-alkyl-COOH, heteroaryl, -C_1-C_6-alkyl-COOH, -O-C_1-C_6-alkyl-COOH, -$S(O)_2R^{51}$, -C_2-C_6-alkenyl-COOH, -OR^{51}, -NO_2, halogen, -COOH, -CF_3, -CN, =O, -$N(R^{51}R^{52})$, wherein the aryl or heteroaryl moieties are optionally substituted with one or more R^{53}.

160. A pharmaceutical composition according to claim 159 wherein R^{50} is C_1-C_6-alkyl, C_1-C_6-alkoxy, aryl, aryloxy, -C(=O)-NR^{50A}-C_1-C_6-alkyl, -C(=O)-NH-$(CH_2CH_2O)_m$$C_1$-$C_6$-alkyl-COOH, aryl-$C_1$-$C_6$-alkoxy , -$OR^{51}$, -$NO_2$, halogen, -COOH, -$CF_3$, wherein any aryl moiety is optionally substituted with one or more R^{53}.

161. A pharmaceutical composition according to claim 160 wherein R^{50} is C_1-C_6-alkyl, aryloxy, -C(=O)-NR^{50A}-C_1-C_6-alkyl, -C(=O)-NH-$(CH_2CH_2O)_m$$C_1$-$C_6$-alkyl-COOH, aryl-$C_1$-$C_6$-alkoxy , -$OR^{51}$, halogen, -COOH, -$CF_3$, wherein any aryl moiety is optionally substituted with one or more R^{53}.

162. A pharmaceutical composition according to claim 161 wherein R^{50} is C_1-C_6-alkyl, ArG1-O-, -C(=O)-NR^{50A}-C_1-C_6-alkyl, -C(=O)-NH-$(CH_2CH_2O)_m$$C_1$-$C_6$-alkyl-COOH, ArG1-$C_1$-

C_6-alkoxy , -OR^{51}, halogen, -COOH, -CF_3, wherein any aryl moiety is optionally substituted with one or more R^{53}.

163. A pharmaceutical composition according to claim 162 wherein R^{50} is -C(=O)-$NR^{50A}CH_2$, -C(=O)-NH-$(CH_2CH_2O)_2CH_2$I-COOH, or -C(=O)-$NR^{50A}CH_2CH_2$.

164. A pharmaceutical composition according to claim 162 wherein R^{50} is phenyl, methyl or ethyl.

165. A pharmaceutical composition according to claim 164 wherein R^{50} is methyl or ethyl.

166. A pharmaceutical composition according to claim 127 wherein m is 1 or 2.

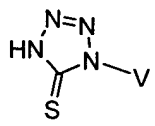
167. A pharmaceutical composition according to claim 127 wherein R^{51} is methyl.

168. A pharmaceutical composition according to claim 127 wherein R^{53} is C_1-C_6-alkyl, C_1-C_6-alkoxy, -OR^{51}, halogen,or -CF_3.

169. A pharmaceutical composition according to claim 127 wherein R^{50A} is -$C(O)OCH_3$, -$C(O)OCH_2CH_3$ -COOH, -$CH_2C(O)OCH_3$, -$CH_2C(O)OCH_2CH_3$, -$CH_2CH_2C(O)OCH_3$, -$CH_2CH_2C(O)OCH_2CH_3$, -CH_2COOH, methyl, or ethyl.

170. A pharmaceutical composition according to claim 127 wherein R^{50B} is -$C(O)OCH_3$, -$C(O)OCH_2CH_3$ -COOH, -$CH_2C(O)OCH_3$, -$CH_2C(O)OCH_2CH_3$, -$CH_2CH_2C(O)OCH_3$, -$CH_2CH_2C(O)OCH_2CH_3$, -CH_2COOH, methyl, or ethyl.

171. A pharmaceutical composition according to claim 1 wherein the zinc-binding ligand is



wherein V is C_1-C_6-alkyl, aryl, heteroaryl, aryl-C_{1-6}-alkyl- or aryl-C_{2-6}-alkenyl-, wherein the alkyl or alkenyl is optionally substituted with one or more substituents independently selected

from R^{54}, and the aryl or heteroaryl is optionally substituted with one or more substituents independently selected from R^{55},

R^{54} is independently selected from halogen, -CN, $-CF_3$, $-OCF_3$, aryl, -COOH and $-NH_2$,

R^{55} is independently selected from

- hydrogen, halogen, -CN, $-CH_2CN$, $-CHF_2$, $-CF_3$, $-OCF_3$, $-OCHF_2$, $-OCH_2CF_3$, $-OCF_2CHF_2$, $-S(O)_2CF_3$, $-OS(O)_2CF_3$, $-SCF_3$, $-NO_2$, $-OR^{56}$, $-NR^{56}R^{57}$, $-SR^{56}$, $-NR^{56}S(O)_2R^{57}$, $-S(O)_2NR^{56}R^{57}$, $-S(O)NR^{56}R^{57}$, $-S(O)R^{56}$, $-S(O)_2R^{56}$, $-OS(O)_2\ R^{56}$, $-C(O)NR^{56}R^{57}$, $-OC(O)NR^{56}R^{57}$, $-NR^{56}C(O)R^{57}$, $-CH_2C(O)NR^{56}R^{57}$, $-OC_1$-C_6-alkyl-$C(O)NR^{56}R^{57}$, $-CH_2OR^{56}$, $-CH_2OC(O)R^{56}$, $-CH_2NR^{56}R^{57}$, $-OC(O)R^{56}$, $-OC_1$-C_8-alkyl-$C(O)OR^{56}$, $-OC_1$-C_6-alkyl-OR^{56}, $-SC_1$-C_6-alkyl-$C(O)OR^{56}$, $-C_2$-C_6-alkenyl-$C(=O)OR^{56}$, $-NR^{56}$-$C(=O)$-C_1-C_6-alkyl-$C(=O)OR^{56}$, $-NR^{56}$-$C(=O)$-C_1-C_6-alkenyl-$C(=O)OR^{56}$, $-C(O)OR^{56}$, or $-C_2$-C_6-alkenyl-$C(=O)R^{56}$,

- C_1-C_6-alkyl, C_2-C_6-alkenyl or C_2-C_6-alkynyl,

  which may optionally be substituted with one or more substituents selected from R^{58},

- aryl, aryloxy, aryloxycarbonyl, aroyl, arylsulfanyl, aryl-C_1-C_6-alkoxy, aryl-C_1-C_6-alkyl, aryl-C_2-C_6-alkenyl, aroyl-C_2-C_6-alkenyl, aryl-C_2-C_6-alkynyl, heteroaryl, heteroaryl-C_1-C_6-alkyl, heteroaryl-C_2-C_6-alkenyl or heteroaryl-C_2-C_6-alkynyl,

  of which the cyclic moieties optionally may be substituted with one or more substituents selected from R^{59},

R^{56} and R^{57} are independently selected from hydrogen, OH, CF_3, C_1-C_{12}-alkyl, aryl-C_1-C_6-alkyl, -$C(=O)$-C_1-C_6-alkyl or aryl, wherein the alkyl groups may optionally be substituted with one or more substituents independently selected from R^{60}, and the aryl groups may optionally be substituted with one or more substituents independently selected from R^{61}; R^{56} and R^{57} when attached to the same nitrogen atom may form a 3 to 8 membered heterocyclic ring with the nitrogen atom, the heterocyclic ring optionally containing one or two further heteroatoms selected from nitrogen, oxygen and sulphur, and optionally containing one or two double bonds,

R^{58} is independently selected from halogen, -CN, $-CF_3$, $-OCF_3$, $-OR^{56}$, and $-NR^{56}R^{57}$,

R^{59} is independently selected from halogen, -C(O)OR^{56}, -CH_2C(O)OR^{56}, -CH_2OR^{56}, -CN, -CF_3, -OCF_3, -NO_2, -OR^{56}, -$NR^{56}R^{57}$ and C_1-C_6-alkyl,

R^{60} is independently selected from halogen, -CN, -CF_3, -OCF_3, -OC_1-C_6-alkyl, -C(O)OC_1-C_6-alkyl, -C(=O)-R^{62}, -COOH and –NH_2,

R^{61} is independently selected from halogen, -C(O)OC_1-C_6-alkyl, -COOH, -CN, -CF_3, -OCF_3, -NO_2, -OH, -OC_1-C_6-alkyl, -NH_2, C(=O) or C_1-C_6-alkyl,

R^{62} is C_1-C_6-alkyl, aryl optionally substituted with one or more substituents independently selected from halogen, or heteroaryl optionally substituted with one or more C_1-C_6-alkyl independently,

or any enantiomer, diastereomer, racemic mixture, tautomer, or salt thereof with a pharmaceutically acceptable acid or base.

172. A pharmaceutical composition according to claim 171 wherein V is aryl, heteroaryl, or aryl-C_{1-6}-alkyl-, wherein the alkyl is optionally substituted with one or more substituents independently selected R^{54}, and the aryl or heteroaryl is optionally substituted with one or more substituents independently selected from R^{55}.

173. A pharmaceutical composition according to claim 172 wherein V is aryl, Het1, or aryl-C_{1-6}-alkyl-, wherein the alkyl is optionally substituted with one or more substituents independently selected from R^{54}, and the aryl or heteroaryl moiety is optionally substituted with one or more substituents independently selected from R^{55}.

174. A pharmaceutical composition according to claim 173 wherein V is aryl, Het2, or aryl-C_{1-6}-alkyl-, wherein the alkyl is optionally substituted with one or more substituents independently selected from R^{54}, and the aryl or heteroaryl moiety is optionally substituted with one or more substituents independently selected from R^{55}.

175. A pharmaceutical composition according to claim 174 wherein V is aryl, Het3, or aryl-C_{1-6}-alkyl-, wherein the alkyl is optionally substituted with one or more substituents independently selected from R^{54}, and the aryl or heteroaryl moiety is optionally substituted with one or more substituents independently selected from R^{55}.

176. A pharmaceutical composition according to claim 175 wherein V is aryl optionally substituted with one or more substituents independently selected from R^{55}.

177. A pharmaceutical composition according to claim 176 wherein V is ArG1 optionally substituted with one or more substituents independently selected from R^{55}.

178. A pharmaceutical composition according to claim 177 wherein V is phenyl, naphthyl or anthranyl optionally substituted with one or more substituents independently selected from R^{55}.

179. A pharmaceutical composition according to claim 178 wherein V is phenyl optionally substituted with one or more substituents independently selected from R^{55}.

180. A pharmaceutical composition according to claim 171 wherein R^{55} is independently selected from

- halogen, C_1-C_6-alkyl, -CN, -OCF_3 ,-CF_3, -NO_2, -OR^{56}, -$NR^{56}R^{57}$, -$NR^{56}C(O)R^{57}$ -SR^{56}, -OC_1-C_8-alkyl-$C(O)OR^{56}$, or -$C(O)OR^{56}$,
- C_1-C_6-alkyl optionally substituted with one or more substituents independently selected from R^{58}
- aryl, aryl-C_1-C_6-alkyl, heteroaryl, or heteroaryl-C_1-C_6-alkyl

of which the cyclic moieties optionally may be substituted with one or more substituents independently selected from R^{59}.

181. A pharmaceutical composition according to claim 180 wherein R^{55} is independently selected from

- halogen, C_1-C_6-alkyl, -CN, -OCF_3 ,-CF_3, -NO_2, -OR^{56}, -$NR^{56}R^{57}$, -$NR^{56}C(O)R^{57}$ -SR^{56}, -OC_1-C_8-alkyl-$C(O)OR^{56}$, or -$C(O)OR^{56}$
- C_1-C_6-alkyl optionally substituted with one or more substituents independently selected from R^{58}
- ArG1, ArG1-C_1-C_6-alkyl, Het3, or Het3-C_1-C_6-alkyl

of which the cyclic moieties optionally may be substituted with one or more substituents independently selected from R^{59}.

182. A pharmaceutical composition according to claim 181 wherein R^{55} is independently selected from halogen, $-OR^{56}$, $-NR^{56}R^{57}$, $-C(O)OR^{56}$, $-OC_1$-C_8-alkyl-$C(O)OR^{56}$, $-NR^{56}C(O)R^{57}$ or C_1-C_6-alkyl.

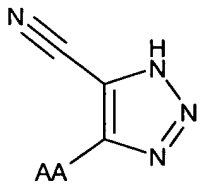
183. A pharmaceutical composition according to claim 182 wherein R^{55} is independently selected from halogen, $-OR^{56}$, $-NR^{56}R^{57}$, $-C(O)OR^{56}$, $-OC_1$-C_8-alkyl-$C(O)OR^{56}$, $-NR^{56}C(O)R^{57}$, methyl or ethyl.

184. A pharmaceutical composition according to claim 171 wherein R^{56} and R^{57} are independently selected from hydrogen, CF_3, C_1-C_{12}-alkyl, or $-C(=O)$-C_1-C_6-alkyl; R^{56} and R^{57} when attached to the same nitrogen atom may form a 3 to 8 membered heterocyclic ring with the nitrogen atom.

185. A pharmaceutical composition according to claim 184 wherein R^{56} and R^{57} are independently selected from hydrogen or C_1-C_{12}-alkyl, R^{56} and R^{57} when attached to the same nitrogen atom may form a 3 to 8 membered heterocyclic ring with the nitrogen atom.

186. A pharmaceutical composition according to claim 185 wherein R^{56} and R^{57} are independently selected from hydrogen or methyl, ethyl, propyl butyl, R^{56} and R^{57} when attached to the same nitrogen atom may form a 3 to 8 membered heterocyclic ring with the nitrogen atom.

187. A pharmaceutical composition according to claim 1 wherein the zinc-binding ligand is



wherein AA is C_1-C_6-alkyl, aryl, heteroaryl, aryl-$C_{1\text{-}6}$-alkyl- or aryl-$C_{2\text{-}6}$-alkenyl-, wherein the alkyl or alkenyl is optionally substituted with one or more substituents independently selected from R^{63}, and the aryl or heteroaryl is optionally substituted with one or more substituents independently selected from R^{64},

R^{63} is independently selected from halogen, -CN, $-CF_3$, $-OCF_3$, aryl, -COOH and $-NH_2$,

R^{64} is independently selected from

- hydrogen, halogen, -CN, -CH_2CN, -CHF_2, -CF_3, -OCF_3, -$OCHF_2$, -OCH_2CF_3, -OCF_2CHF_2, -$S(O)_2CF_3$, -$OS(O)_2CF_3$, -SCF_3, -NO_2, -OR^{65}, -$NR^{65}R^{66}$, -SR^{65}, -$NR^{65}S(O)_2R^{66}$, -$S(O)_2NR^{65}R^{66}$, -$S(O)NR^{65}R^{66}$, -$S(O)R^{65}$, -$S(O)_2R^{65}$, -$OS(O)_2$ R^{65}, -$C(O)NR^{65}R^{66}$, -$OC(O)NR^{65}R^{66}$, -$NR^{65}C(O)R^{66}$, -$CH_2C(O)NR^{65}R^{66}$, -OC_1-C_6-alkyl-$C(O)NR^{65}R^{66}$, -CH_2OR^{65}, -$CH_2OC(O)R^{65}$, -$CH_2NR^{65}R^{66}$, -$OC(O)R^{65}$, -OC_1-C_6-alkyl-$C(O)OR^{65}$, -OC_1-C_6-alkyl-OR^{65}, -SC_1-C_6-alkyl-$C(O)OR^{65}$, –C_2-C_6-alkenyl-$C(=O)OR^{65}$, -NR^{65}-$C(=O)$-C_1-C_6-alkyl-$C(=O)OR^{65}$, -NR^{65}-$C(=O)$-C_1-C_6-alkenyl-$C(=O)OR^{65}$, -$C(O)OR^{65}$, or –C_2-C_6-alkenyl-$C(=O)R^{65}$,

- C_1-C_6-alkyl, C_2-C_6-alkenyl or C_2-C_6-alkynyl, each of which may optionally be substituted with one or more substituents selected from R^{67},

- aryl, aryloxy, aryloxycarbonyl, aroyl, arylsulfanyl, aryl-C_1-C_6-alkoxy, aryl-C_1-C_6-alkyl, aryl-C_2-C_6-alkenyl, aroyl-C_2-C_6-alkenyl, aryl-C_2-C_6-alkynyl, heteroaryl, heteroaryl-C_1-C_6-alkyl, heteroaryl-C_2-C_6-alkenyl or heteroaryl-C_2-C_6-alkynyl,

of which the cyclic moieties optionally may be substituted with one or more substituents selected from R^{68},

R^{65} and R^{66} are independently selected from hydrogen, OH, CF_3, C_1-C_{12}-alkyl, aryl-C_1-C_6-alkyl, -$C(=O)$-R^{69}, aryl or heteroaryl, wherein the alkyl groups may optionally be substituted with one or more substituents selected from R^{70}, and the aryl and heteroaryl groups may optionally be substituted with one or more substituents independently selected from R^{71}; R^{65} and R^{66} when attached to the same nitrogen atom may form a 3 to 8 membered heterocyclic ring with the said nitrogen atom, the heterocyclic ring optionally containing one or two further heteroatoms selected from nitrogen, oxygen and sulphur, and optionally containing one or two double bonds,

R^{67} is independently selected from halogen, -CN, -CF_3, -OCF_3, -OR^{65}, and -$NR^{65}R^{66}$,

R^{68} is independently selected from halogen, -$C(O)OR^{65}$, -$CH_2C(O)OR^{65}$, -CH_2OR^{65}, -CN, -CF_3, -OCF_3, -NO_2, -OR^{65}, -$NR^{65}R^{66}$ and C_1-C_6-alkyl,

R^{69} is independently selected from C_1-C_6-alkyl, aryl optionally substituted with one or more halogen, or heteroaryl optionally substituted with one or more C_1-C_6-alkyl,

R^{70} is independently selected from halogen, -CN, -CF_3, -OCF_3, -OC_1-C_6-alkyl, -$C(O)OC_1$-C_6-alkyl, -COOH and –NH_2,

R^{71} is independently selected from halogen, -$C(O)OC_1$-C_6-alkyl, -COOH, -CN, -CF_3, -OCF_3, -NO_2, -OH, -OC_1-C_6-alkyl, -NH_2, C(=O) or C_1-C_6-alkyl,

or any enantiomer, diastereomer, racemic mixture, tautomer, or salt thereof with a pharmaceutically acceptable acid or base.

188. A pharmaceutical composition according to claim 187 wherein AA is aryl, heteroaryl or aryl-C_{1-6}-alkyl-, wherein the alkyl is optionally substituted with one or more R^{63}, and the aryl or heteroaryl is optionally substituted with one or more substituents independently selected from R^{64}.

189. A pharmaceutical composition according to claim 188 wherein AA is aryl or heteroaryl optionally substituted with one or more substituents independently selected from R^{64}.

190. A pharmaceutical composition according to claim 189 wherein AA is ArG1 or Het1 optionally substituted with one or more substituents independently selected from R^{64}.

191. A pharmaceutical composition according to claim 190 wherein AA is ArG1 or Het2 optionally substituted with one or more substituents independently selected from R^{64}.

192. A pharmaceutical composition according to claim 191 wherein AA is ArG1 or Het3 optionally substituted with one or more substituents independently selected from R^{64}.

193. A pharmaceutical composition according to claim 192 wherein AA is phenyl, naphtyl, anthryl, carbazolyl, thienyl, pyridyl, or benzodioxyl optionally substituted with one or more substituents independently selected from R^{64}.

194. A pharmaceutical composition according to claim 193 wherein AA is phenyl or naphtyl optionally substituted with one or more substituents independently selected from R^{64}.

195. A pharmaceutical composition according to claim 187 wherein R^{64} is independently selected from hydrogen, halogen, $-CF_3$, $-OCF_3$, $-OR^{65}$, $-NR^{65}R^{66}$, C_1-C_6-alkyl , $-OC(O)R^{65}$, $-OC_1$-C_6-alkyl-$C(O)OR^{65}$, aryl-C_2-C_6-alkenyl, aryloxy or aryl, wherein C_1-C_6-alkyl is optionally substituted with one or more substituents independently selected from R^{67}, and the cyclic moieties optionally are substituted with one or more substituents independently selected from R^{68}.

196. A pharmaceutical composition according to claim 195 wherein R^{64} is independently selected from halogen, $-CF_3$, $-OCF_3$, $-OR^{65}$, $-NR^{65}R^{66}$, methyl, ethyl, propyl, $-OC(O)R^{65}$, $-OCH_2$-$C(O)OR^{65}$, $-OCH_2$-CH_2-$C(O)OR^{65}$, phenoxy optionally substituted with one or more substituents independently selected from R^{68}.

197. A pharmaceutical composition according to claim 187 wherein R^{65} and R^{66} are independently selected from hydrogen, CF_3, C_1-C_{12}-alkyl, aryl, or heteroaryl optionally substituted with one or more substituents independently selected from R^{71}.

198. A pharmaceutical composition according to claim 197 wherein R^{65} and R^{66} are independently hydrogen, C_1-C_{12}-alkyl, aryl, or heteroaryl optionally substituted with one or more substituents independently selected from R^{71}.

199. A pharmaceutical composition according to claim 198 wherein R^{65} and R^{66} are independently hydrogen, methyl, ethyl, propyl, butyl, 2,2-dimethyl-propyl, ArG1 or Het1 optionally substituted with one or more substituents independently selected from R^{71}.

200. A pharmaceutical composition according to claim 199 wherein R^{65} and R^{66} are independently hydrogen, methyl, ethyl, propyl, butyl, 2,2-dimethyl-propyl, ArG1 or Het2 optionally substituted with one or more substituents independently selected from R^{71}.

201. A pharmaceutical composition according to claim 200 wherein R^{65} and R^{66} are independently hydrogen, methyl, ethyl, propyl, butyl, 2,2-dimethyl-propyl, ArG1 or Het3 optionally substituted with one or more substituents independently selected from R^{71}.

202. A pharmaceutical composition according to claim 201 wherein R^{65} and R^{66} are independently hydrogen, methyl, ethyl, propyl, butyl, 2,2-dimethyl-propyl, phenyl, naphtyl, thiadiazolyl optionally substituted with one or more R^{71} independently; or isoxazolyl optionally substituted with one or more substituents independently selected from R^{71}.

203. A pharmaceutical composition according to claim 187 wherein R^{71} is halogen or C_1-C_6-alkyl.

204. A pharmaceutical composition according to claim 203 wherein R^{71} is halogen or methyl.

205. A pharmaceutical composition according to claim 1 wherein the insulin is rapid acting insulin.

206. A pharmaceutical composition according to claim 1 wherein the insulin is selected from the group consisting of human insulin, an analogue thereof, a derivative thereof, and combinations of any of these.

207. A pharmaceutical composition according to claim 206 wherein the insulin is an analogue of human insulin selected from the group consisting of

iii. An analogue wherein position B28 is Asp, Lys, Leu, Val, or Ala and position B29 is Lys or Pro; and

iv. des(B28-B30), des(B27) or des(B30) human insulin.

208. A pharmaceutical composition according to claim 207, wherein the insulin is an analogue of human insulin wherein position B28 is Asp or Lys, and position B29 is Lys or Pro.

209. A pharmaceutical composition according to claim 207 wherein the insulin is des(B30) human insulin.

210. A pharmaceutical composition according to claim 207 wherein the insulin is is an analogue of human insulin wherein position B3 is Lys and position B29 is Glu or Asp.

211. A pharmaceutical composition according to claim 206 wherein the insulin is a derivative of human insulin having one or more lipophilic substituents.

212. A pharmaceutical composition according to claim 211 wherein the insulin derivative is selected from the group consisting of B29-N$^{\varepsilon}$-myristoyl-des(B30) human insulin, B29-N$^{\varepsilon}$-palmitoyl-des(B30) human insulin, B29-N$^{\varepsilon}$-myristoyl human insulin, B29-N$^{\varepsilon}$-palmitoyl human insulin, B28-N$^{\varepsilon}$-myristoyl Lys^{B28} Pro^{B29} human insulin, B28-N$^{\varepsilon}$-palmitoyl Lys^{B28} Pro^{B29} human insulin, B30-N$^{\varepsilon}$-myristoyl-Thr^{B29}Lys^{B30} human insulin, B30-N$^{\varepsilon}$-palmitoyl-Thr^{B29}Lys^{B30} human insulin, B29-N$^{\varepsilon}$-(N-palmitoyl-γ-glutamyl)-des(B30) human insulin, B29-N$^{\varepsilon}$-(N-lithocholyl-γ-glutamyl)-des(B30) human insulin, B29-N$^{\varepsilon}$-(ω-carboxyheptadecanoyl)-des(B30) human insulin and B29-N$^{\varepsilon}$-(ω-carboxyheptadecanoyl) human insulin.

213. A pharmaceutical composition according to claim 212 wherein the insulin derivative is B29-N$^{\varepsilon}$-myristoyl-des(B30) human insulin.

214. A pharmaceutical composition according to claim 1 comprising 2-6 moles zinc^{2+} ions per mole insulin.

215. A pharmaceutical composition according to claim 214 comprising 2-3 moles zinc^{2+} ions per mole insulin.

216. A pharmaceutical composition according to claim 1 further comprising at least 3 molecules of a phenolic compound per insulin hexamer.

217. A pharmaceutical composition according to claim 1 further comprising an isotonicity agent.

218. A pharmaceutical composition according to claim 1 further comprising a buffer substance.

219. A method of stabilising an insulin composition comprising adding a zinc-binding ligand according to claim 1 to the insulin composition.

220. A method of treating type 1 or type 2 diabetes comprising administering to a patient in need thereof a pharmaceutically effective dose of an insulin composition according to claim 1.